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(54) Title: SYSTEM FOR COLLECTION OF DATA AND IDENTIFICATION OF UNKNOWN ION SPECIES IN AN ELECTRIC FIELD
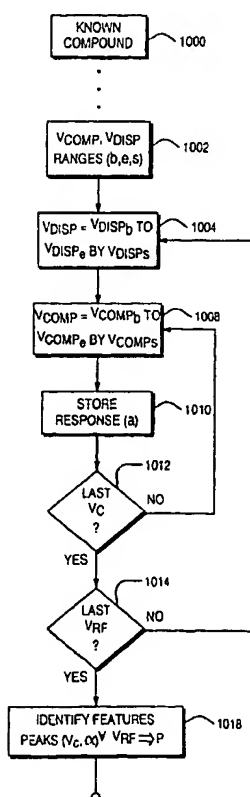
(57) Abstract: An apparatus for identification of chemical species by measurement of mobility as a function of high electric field and for generating unique compound-dependent signatures based on ion mobility at a plurality of peak RF voltages for a given compensation. The resulting detection data is compared against a library of data in order to identify a detected chemical species.

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SYSTEM FOR COLLECTION OF DATA AND IDENTIFICATION OF UNKNOWN ION SPECIES IN AN ELECTRIC FIELD

BACKGROUND OF THE INVENTION

5   The present invention relates generally to identification of unknown members of a sample by mobility characteristics, and more particularly to devices that analyze compounds via high field asymmetric waveform ion mobility spectrometry.

There are a number of different circumstances in which it is desirable to
10   perform a chemical analysis to identify compounds in a sample. Such samples may be taken directly from the environment or they may be provided by front end specialized devices to separate or prepare compounds before analysis. Unfortunately, recent events have seen members of the general public exposed to dangerous chemical compounds in situations where previously no thought
15   was given to such exposure. There exists, therefore, a demand for low cost, accurate, easy to use, and reliable devices capable of detecting the chemical makeup of a sample.

One class of known chemical analysis instruments are mass spectrometers. Mass spectrometers are generally recognized as being the most
20   accurate type of detectors for compound identification, given that they can generate a fingerprint pattern for even fragment ions. However, mass spectrometers are quite expensive, easily exceeding a cost of $100,000 or more and are physically large enough to become difficult to deploy everywhere the public might be exposed to dangerous chemicals. Mass spectrometers also
25   suffer from other shortcomings such as the need to operate at relatively low pressures, resulting in complex support systems. They also need a highly trained

operator to tend to and interpret the results. Accordingly, mass spectrometers - are generally difficult to use outside of laboratories.

A class of chemical analysis instruments more suitable for field operation is known as are known as Field Asymmetric Ion Mobility

5   Spectrometers (FAIMS), also known as Radio Frequency Ion Mobility Spectrometers (RFIMS) among other names. This type of spectrometer subjects an ionized gas sample to a varying high-low asymmetric electric field and filters ions based on their field mobility.

The gas sample flows through a field which allows only selected ion

10   species to pass through, according to the compensation voltage, and specifically only those ions that exhibit particular mobility responses to the field. An ion detector then collects detection intensity data for the detected ions. The intensity data exhibit attributes such as "peaks." These peaks are interpreted according to the compensation voltage at which a species of ion is able to pass

15   through an asymmetric field of set field parameters.

A typical FAIMS device includes a pair of electrodes in a drift tube. An asymmetric field is applied to the electrodes across the ion flow path. The asymmetric RF field, as shown in Fig. 1A, alternates between a high or "peak" field strength and a low field strength. The field varies with a particular time

20   period, t, (frequency) and duty cycle d. Field strength, E, varies as the applied voltage V and size of the gap between electrodes. Ions will pass through the gap between the electrodes only when their net transverse displacement per period of the asymmetric field is zero; in contrast, ions that undergo a net displacement will eventually undergo collisional neutralization on one of the

25   electrodes. In a given Radio Frequency (RF) asymmetric field, a displaced ion can be restored to the center of the gap (i.e. compensated, with no net displacement for that ion) when a low strength DC electric field (the compensation voltage, Vcomp) is superimposed on the RF. Ions with differing displacement (owing to characteristic dependence of mobility in the high field

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condition) can be passed through the gap at compensation voltages characteristic of a particular ion and this is accomplished by applying various strengths of Vcomp. In this case, this system can function as continuous ion filter; or a scan of Vcomp will allow complete measure of ion species in the

5   analyzer. The recorded image of the spectral scan of the sample is sometimes referred to as a "mobility scan" or as an "ionogram").

Examples of mobility scans based on the output from a FAIMS device are shown in Figs. 1B-1 and 1B-2. The compounds analyzed here consisted of acetone and an isomer of xylene (o-xylene). In the first case (Fig. 1B-1) a

10   single compound, acetone, was independently applied to the FAIMS analyzer. The illustrated plot is typical of the observed response of the FAIMS device, with an intensity of detected ions dependent on the compensation voltage (Vcomp). For example, the acetone sample exhibited a peak intensity response at a compensation voltage of approximately –2 volts.

15   Fig. 1B-2 illustrates the results when analyzing a mixture of the two compounds, here, acetone and o-xylene. The combined response shows two peaks in approximately the same region as for the independent case. The compounds in the mixture can therefore be detected by comparing the response against the library, for example, of stored known responses for independently

20   analyzed compounds, or libraries of mixtures. Thus, the independently analyzed compounds shown in Fig. 1B-1 can be stored in a computer system, and when compound responses such as that in Fig. 1B-2 are observed, the relative locations of the peaks can be compared against the stored responses in the library to determine the constitution of the mixture.

25   A problem occurs, however, especially with FAIMS devices, in that relatively complex samples can be very difficult to detect. First of all, the peaks as seen in the typical FAIMS spectra are generally broad in width. Therefore, compounds having similar peak compensation voltages may therefore be difficult to separate from one another. Indeed, there may be particular

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conditions where two different chemicals actually exhibit the same
compensation voltage at a given maximum intensity for the applied asymmetric
RF voltage (referred to here as peak RF voltage). In such a case, it is not
possible to resolve between two different chemicals at all. Another problem

5   may occur when two or more chemical species have the same or almost the
same mobility. This is most likely to happen in the low electric field regime
where most existing ion mobility spectrometer systems operate. Therefore, if
two or more chemical species have the same or almost the same mobility, then
their spectroscopic peaks will overlap, and identification and quantification of

10   individual species will be difficult or impossible.

A specific RF level and compensation voltage will permit only a
particular species of ion (according to mobility) to pass through the filter to the
detector. By noting the RF level and compensation voltage and the
corresponding detected signal, various ion species can be identified, as well as

15   their relative concentrations (as seen in the peak characteristics).

Consider a plot of mobility dependence on electric field, as shown in
Fig. 1C. This figure mobility versus electric field strength for three examples of
ions, with field dependent mobility (expressed as the coefficient of high field
mobility, α) shown for species at greater, equal to and less than zero. The

20   velocity of an ion can be measured in an electric field, E, low enough so that
velocity, V, is proportional to the electrical field as V=KE through a coefficient,
K, called the coefficient of mobility. K can be shown to be theoretically related
to the ion species and gas molecular interaction properties. This coefficient of
mobility is considered to be a unique parameter that enables the identification of

25   different ion species and is determined by, ion properties such as charge, size,
and mass as well as the collision frequency and energy obtained by ions
between collisions.

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When the ratio of E/N is small, K is constant in value, but at increasing E/N values, the coefficient of mobility begins to vary. The effect of the electric field can be expressed approximately as

$$K(E) = K(0)[1+\alpha(E)]$$

5 where $K(0)$ is a low voltage coefficient of mobility, and α is a specific parameter showing the electric field dependence of mobility for a specific ion.

Thus, as exhibited in Fig. 1C, at relatively low electric field strengths, of say less than approximately 8,000 volts per centimeter (V/cm), multiple ions may have the same mobility. However, as the electric field strengths increase,

10 the different species diverge in their response such that their mobility varies as a function of the applied electric field. This is a clear expression of the fact that ion mobility is independent of applied electric field at relatively low field strengths but is field-dependent at higher applied field strengths.

Fig. 1B demonstrates that each species can have a unique behavior in

15 high fields according to its mobility characteristics. The ions passing through the filter are detected downstream. The detection signal intensity can be plotted, resulting in display of a characteristic detection peak for a given RF and Vcomp. Peak intensity, location, and shape are typically used for species identification.

20 However, a problem occurs, especially with FAIMS devices, in that relatively complex samples can be very difficult to discriminate. First of all, the peaks as seen in the typical FAIMS spectra are generally broad in width. Therefore, compounds having similar peak compensation voltages may be difficult to separate from one another. Indeed, there may be particular

25 conditions where two different chemicals actually exhibit the same peak at the same compensation voltage at a given asymmetric RF field.

For example in Fig. 1D, there are four compounds each with a unique characteristic mobility curve that expresses the mobility dependence associated with that compound at each of various peak RF values and compensation

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voltage levels. Four different chemical compounds are shown, including lutidine, cyclohexane, benzene, and a chemical agent simulant dimethyl-methyl-phosphonate (DMMP). Each curve shows detection peaks at the various field conditions that in total are characteristic for the compound. As shown, there is a

5   region 100 in which the mobility curves for DMMP and cyclohexane overlap with one another. Therefore, operating in a peak RF voltage region of from approximately 2,500 to 2,650 volts, at around -6 to -8 volts compensation, one would find it impossible to discriminate between the two compounds upon a single scan. In other words, the conventional spectral scan would plot the

10   overlapping peaks as a single peak at that field condition.

A cylindrical FAIMS device is described in US patent number 5,420,424, where the amplitude of the asymmetric periodic potential is in the range of about 1 to 6 Kv or 2 to 5 Kv, and preferably at about 3 Kv, depending on the ionic species of interest. After the magnitude of the asymmetric voltage

15   has been set, the compensation voltage is held constant or scanned to provide separation of the ionic species.

Even with these improvements, ion species detection is not error free, especially with complex sample mixtures. False negatives are dangerous, and false positives can be expensive and reduce trust in the device. This can be very

20   serious where harmful compounds are being monitored. It is also desirable to have a fast and simple apparatus to achieve such detections with improved accuracy.

SUMMARY OF THE INVENTION

25   The present invention is directed to a method and system for identification of unknown species of ions traveling through an asymmetric excitation field, the identification being based on the known characteristic mobility behavior of ion species under known field conditions.

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Illustrative apparatus of the invention includes an ionization section, a filter section, a detection section, an identification section, and a controller section. The controller (e.g., microprocessor, laptop, etc.) may typically incorporate the identification section (lookup table, comparator, etc.).

5   In practice of the invention, we disclose innovations for isolating ion species of interest in a sample and positively identifying the species with a high degree of reliability. We apply techniques for improving the detection and identification processes. This process may also include separating the ions from background noise or from other ion species in the sample.

10   In one significant aspect, the present invention intentionally controls and uses changes of the filter field (i.e., changes in "field conditions") for better revealing and isolating ion species in the sample. The ionization and filter sections may assume many different physical forms.

As ions are passed through the filter, they deposit charges at a detector.
15   The intensity of the detection is then recorded against the compensation voltage (Vcomp) for a set RF condition (Vrf). Spectral peaks may also be determined while Vcomp is scanned through a range.

The present invention then takes this process further. Specifically, we have identified stratagem for improving species discrimination by intentionally
20   controlling field conditions in a manner that results in improved isolation of ion species. In one embodiment, this involves detecting ion species behavior in response to at least two different applied RF field strengths, and thus at two different sets of field conditions. At each ion species detection we associate the applied compensation and RF with the detection signal and match or correlate
25   this with known data to identify the detected ion species.

Several methods of adjusting field conditions may be used, including adjusting field strength, frequency, aspects of the waveform asymmetry, pulse shape, duty cycle, and the like, to effect meaningful changes in field conditions that affect ion mobility. These alternatives are selected for the ability they

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provide in separating and isolating ion species in the sample. This assumes that the ion species are sensitive to such changes. As long as there is a desirable effect on the mobility behavior of the ions in the field then we can make use of this control. In all events these controls are directed to causing one species to

5   behave differently from another species in the field so that a more refined or better defined set of ions can be passed to the detector.

Therefore, for purposes of this invention, we define "field conditions" and "set of field conditions" as any combination of compensation and RF established in the gap between the filter electrodes as may affect ion mobility.

10   Field conditions are considered to be different when attributes of the RF or compensation have been changed, whether this takes the form of adjustment in frequency, intensity, asymmetry, periodicity, pulse shape or similar variables. Nevertheless, we can control the field conditions and the energy in the field in a manner that has differential effect upon ion mobility in the field. We use this

15   differential effect in controlling ion filtering. In a preferred embodiment, "field conditions" also will be understood to take into account various other aspects such as temperature, flow rate, pressure, and flow volume in the filter, as well as the nature of the carrier gas, if any.

Field conditions can be controlled by several techniques in practice of

20   the invention. For example, frequency has an effect on the 'selectivity' (width) of the output scanned peaks. This can be implemented by changing the value of a fixed operating frequency or by dynamic frequency modulation where a range of frequencies could be scanned, for example. Control of pulse shape, i.e., square, triangular, sinusoidal, ramp, also may be adjusted, where shape may be

25   used to affect response of the ion in the field in a known manner. Magnetic fields may also be used to control flow of ions according to known response characteristics.

The compensation voltage Vcomp may be a separate DC voltage or it may be imposed on the RF signal Vrf, such as by varying the duty cycle. The

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term compensation therefore will be understood as an adjustment to the field by bias voltage or other means that enables tuning the field to pass a desired species of ion to the detector. When we run a spectral scan, we normally scan the compensation voltage through a range of values. However, varying the duty

5   cycle or pulse width can have an effect similar to adjusting or scanning the compensation voltage. The latter can be accomplished by holding the pulse width constant while varying the frequency or by holding the frequency constant while varying the pulse width. We also can apply techniques of pulse amplitude modulation, which is yet another method for generating and adjusting

10   the compensation. Alternatively, with a fixed pulse amplitude, compensation can be generated by varying baseline voltage. These controls can be produced with analog circuitry or can be generated digitally. These and still other control strategies are within the spirit and scope of the invention as will appear to a person skilled in the art.

15   We therefore exercise our ability to control ion behavior in the electric field by.control of field conditions, knowing that different ion species will pass through the filter depending upon these field conditions. In one example, we set the field strength, e.g., amplitude of the RF signal, and then adjust or shift the compensation to a level needed to detect an ion species. If we detect a peak at

20   this set of field conditions, we take this detection data (noting detection peak and field conditions), and then compare this to a store of mobility behavior of known ion species. Upon finding a match or near match, we can make a reliable identification of the species of the detected ions.

             We further exercise field control to distinguish between multiple

25   detection data that may require further clarity. Thus at one set of field conditions some peaks may seem to overlap, but after making a field adjustment such as changing field strength or compensation, these overlapping peaks will be separated and be separately processable as will enable separate identification of the species each represents. Detections thus proceed where detection data

and field conditions are correlated with stored data to make positive species identifications.

It will be appreciated by a person skilled in the art that a "reactant ion peak" (RIP) may be detected in a FAIMS device and will be associated with ions that result from ionization of the background environment in the drift tube. This background may include molecules of carrier gas that are ionized, and perhaps also water molecules that become protonated, during the ionization process. Peaks associated with detection of these ions are referred to as "reactant ion peaks" as opposed to peaks associated with detection of chemical ions of interest.

In practice of the present invention, in one example, increasing the RF field strength typically has a much more dramatic effect on the background RIP than on a sample ion species; as a result of sampling at two or more of a series of different field conditions (whether the difference is in the RF field or the compensation), the RIP peak can be shifted away from the peak for an ion species of interest.

This separation of detection data isolates the ion species of interest from the background detection data and results in a cleaner and more accurate species detection and identification. In this manner, detection accuracy is improved and false positives are reduced in practice of the invention.

Furthermore, intentionally changing or scanning across a range of field conditions can cause the peaks associated with complex or clustered compounds to shift away from peaks associated with monomers in a sample. This enable better species isolation. Furthermore, with sufficient increase in field strength, clustered compounds will even tend to decluster and resolve into identifiable constituents. Therefore, a single complex compound may be identified by its characteristic component ions or sub-clusters, again based on comparison of field conditions and detection data compared to a known data store.

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In embodiments of the invention, we control ionization, such as by increasing ionization energy and fragmenting the sample into characteristic component parts. This increases specificity of the detection data. In other embodiments, we increase the RF energy in the filter section to accomplish

5   fragmentation. This again enables component parts of a sample to be separately detected, the combination of detections enabling us to more accurately identify the ion species in the sample. Thus we can control actions in the ionization section or in the filter section to favorably impact the quality of the detection signal.

10   In the detector region, we note the field conditions in the filter section (as well as ionization and flow) and then we correlate this with detection intensity data. This characterizes an ion species detection of unknown type. This detection data is compared to stored detector data for known species at known filed conditions and a detection identification is made. This approach is

15   simplified, but may be adequate for various embodiments of the invention.

However, in practice of further embodiments of the invention, we also do further processing of the detection signal using techniques such as by evaluating peak spectral energy, generating mobility curves, curve matching, and the like. This enables a more definitive detection process.

20   In one practice of the invention, a detection is made of an ion species at at least two field conditions. Identification is made by collecting multiple detection data representing a signature of the detected ion species in these field conditions, and then by comparing this signature data to a store of known species signatures. The ion species to be identified may be traveling alone or in

25   a group of ions of same or differing characteristic mobility behavior. Nevertheless, we can achieve species-specific isolation and identification.

In yet another embodiment, a FAIMS device operates simultaneously in both positive ion detection mode ("positive mode" or "positive ion mode") and negative ion detection mode ("negative mode" or "negative ion mode") for

complete real-time sample analysis. Alternatively, two separate FAIMS devices may operate in tandem, one in each mode, and detection results can be processed either seriatim or simultaneously and combined for complete real-time sample analysis.

5   A preferred method and apparatus detects multiple species simultaneously based on both ion mobility and ion polarity. A preferred method and apparatus of the invention includes a planar FAIMS spectrometer applied to filtering and simultaneous transport and detection of positive and negative ion species from a sample including mercaptans and other sulfur-containing

10   compounds, and air, methane or other gases.

In one practice of the invention, a compensated asymmetric high RF field is used to separate sulfur-containing compounds (such as mercaptans) from a hydrocarbon background (such as methane). The sample is ionized and the ions representing sulfur-containing compounds (such as mercaptans) are

15   detected according to polarity (i.e., for the most part as negative ions). The hydrocarbons are detected according to polarity (i.e., for the most part as positive ions) in the same device. These detections may even be performed simultaneously where dual detectors are oppositely biased.

In one specific end use, the invention enables detection of trace amounts

20   (ppm, ppb, ppt) of mercaptan in varying and even high hydrocarbon backgrounds. The device is also able to characterize the hydrocarbon gas backgrounds. A preferred practice of the invention has the ability to detect trace amounts of sulfur-containing compounds (e.g., mercaptans) in varying and even high hydrocarbon backgrounds and to characterized the hydrocarbon

25   backgrounds in the same device simultaneously.

In this embodiment of the invention, a gas sample having sulfur-containing compounds (e.g., mercaptans) and methane (or other gases including air) are ionized and flowed through a FAIMS filter. Negative ions are detected indicative of the concentration and identity of the sulfur-containing compounds.

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The same test is run again and positive ions are detected indicative of the hydrocarbon gas in the sample.

These compounds are passed by the FAIMS filter based on their mobility behavior and their having similar trajectories in the presence of
5   compensated electric filter fields. The passed ions are then further separated based on polarity, wherein, for example, mercaptans can be distinguished from a gas such as air or methane. In the negative mode, mercaptans are detected and in the positive mode, the gas (e.g., methane) is distinguished from the mercaptans. Both modes can be run simultaneously.

10   It will thus be appreciated that it has been found generally that samples such as hydrocarbon gas will separate into predominantly positive ion species and sulfur-containing compounds (e.g., mercaptans) will separate into predominantly negative ion species. The preferred planar FAIMS spectrometer is a simple and low cost device, which can perform substantive quantitative
15   analysis of complex mixtures having sulfur-containing compounds (e.g., mercaptans) in a gas, such as hydrocarbon or air.

In practice of the invention, a single positively biased detector electrode downstream from the filter will detect the negatively charged ion stream (negative mode). A single negatively biased detector electrode downstream
20   from the filter will detect the positively charged ion stream (positive mode). A detection signal is generated as these ions deposit their charges on a detector electrode. These detections can be correlated with the RF signal, compensation voltage and detector bias, to identify the detected ion species.

Where two detector electrodes are provided downstream, each
25   oppositely biased, both positive and negatively charged ion species can be detected and identified. In one practice of the invention, where mercaptans were detected in hydrocarbon background, the asymmetric voltage applied to the ion filter electrodes ranged from about 900 to about 1.5 kV (high field condition), and a low voltage of about -400 to -500 V (low field condition). The

frequency ranged 1-2 MHz and the high frequency had an approximate 30% duty cycle, although other operating ranges are possible. In one embodiment, the detector electrodes were biased at +5v and -5v. Now the mercaptans are detected in the negative mode and the hydrocarbon gases can be detected in the

5   positive mode.

The above identification process, while remarkably powerful and useful, may in some applications be substantially improved and simplified by incorporation and use of α parameter (coefficient of high field mobility) information and α curves as part of positive, highly reliable, identification

10   process using unique mobility signatures.

Furthermore, we have found that the field-dependent mobility of a species can be expressed as an α function. In point of fact, the coefficient of field-dependent mobility, α, for a species is expressed as a function of the electric field. The resulting curve showing the experienced mobility or "α"

15   curve, is a unique signature for that species. Furthermore, this signature can be expressed in a device-independent function.

The characteristic mobility for each species can be plotted at multiple field conditions (i.e., detection intensity noted at a series of field conditions), and this and can be expressed as a unique "α function" that identifies the ion

20   species uniquely.

We note that use of the field mobility dependence coefficient α for a single set of field conditions does not necessarily result in a unique identification, because multiple different species can happen to have the same mobility in that single set of field conditions. We have found however that

25   obtaining multiple α data sets for a detected species enables us to uniquely identify that species by its computed "α curve" even when it is indistinguishable from other species in one set of field conditions.

In one practice of the invention, we use the α function to make unique identification of a specific ion species in a sample by using two closely related

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detection data sets (i.e., noting detection intensity at two different but close sets
of field conditions). We use these related sets of field condition values as two
points on a curve, and from which we generate the slope and sign of the curve.
We then can associate sign and slope with each detection and can compare to
5   stored known detection results. Thus we can identify a detected ion species
(with two detections) according to its associated mobility curve. Furthermore,
we have determined that this mobility curve is species specific, and we have
further identified a process for making such identification device-independent.
In any case, we compare detected and computed data to a store of known data to
10   make positive identification of the species of detected ions.

The system of the present invention (which may be expressed as either
method and/or apparatus) is for identification of species of unknown ions that
travel through a varying excitation field. The field is characterized as having
varying influence upon the mobility behavior of the species (single or plural) of
15   ions (single or plural) traveling through the field. The identification of the
detected ion(s) is based on correlating the field-dependent mobility behavior of
the detected ion(s) to a store of known field-dependent mobility behavior(s) of
at least one known species.

We can scan at multiple field conditions to obtain multiple detection
20   peaks. We can also fragment, decluster, or use dopants to control or generate
additional or clarify existing detection peaks as needed. We can use these
alternative to generate multiple detection data for a particular situation, and this
data is processed using various evaluation strategies, such as curve/peak
matching, etc., and then we do a lookup comparison for positive identification
25   of the species of the detected ion(s). A match enables positive identification of
a detected ion species in a sample.

BRIEF DESCRIPTION OF THE DRAWINGS

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The foregoing and other objects, features and advantages of the invention will be apparent from the following more particular description of preferred embodiments of the invention, as illustrated in the accompanying drawings in which like reference characters refer to the same parts throughout

5   the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating the principles of the invention.

Fig. 1A illustrates an asymmetric field having a peak RF, time period, and duty cycle.

Figs. 1B-1 and 1B-2 are a typical display of detected abundance versus

10   applied compensation voltage for a given field strength in a field asymmetric ion mobility spectrometer, first for acetone alone and second for a combination of o-xylene and acetone (Prior Art).

Fig. 1C is a plot of mobility dependence upon electric field strength for three different compounds (Prior Art).

15   Fig. 1D is a plot showing peak detections across a range of combinations of peak Radio Frequency (RF) voltage and compensation voltage for four different compounds (Prior Art).

Fig. 2 is a schematic of a preferred planar field asymmetric ion mobility spectrometer in practice of the present invention.

20   Figs. 3A and 3B illustrate positive and negative mode spectra for different amounts of ethyl mercaptan in practice of the present invention.

Figs. 3C through 3G illustrate the affect of changes in field conditions, such as changes in compensation, on specific spectra, and showing divergent behavior of monomer and reactant ion peak (RIP) detections with changes in

25   field for detecting sulfur hexafluoride (SF6) in practice of the invention.

Figs. 4A and 4B illustrate changes in peak location change in compensation in practice of the present invention.

Figs. 5A and 5B illustrate ability to discriminate between detected ion species by changes in field conditions in practice of the present invention.

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Figs. 6A and 6B illustrate the affect of changes in field conditions, such as changes in compensation, on specific spectra, and showing divergent behavior of monomer, cluster, and reactant ion peak (RIP) detections with changes in field for hexanone and octanone in practice of the present invention.

5   Fig. 7 illustrates effect of changes in field conditions on location of individual detection peaks and ability to separate peaks in practice of the present invention.

Figs. 8A and 8B respectively show a plot of compensation versus field strength for detected monomer and cluster ion peaks for a family of ketones in

10   practice of the present invention.

Fig. 8C includes Table 1, which is a collection of detection data from which the curves of Fig. 8A and 8B were generated for a group of monomer and dimers (clusters) for eight ketones in practice of the present invention.

Figs. 9A and 9B illustrate the results of calculating normalized alpha

15   parameter curves in practice of the present invention.

Fig. 10A shows a sequence of steps of a computer process used to acquire data concerning a particular chemical ion species in practice of the present invention.

Fig. 10B shows a diagram of one possible data structure for a library of

20   stored compound data measurement information in practice of the present invention.

Fig. 10C is a series of steps that may be applied to perform a chemical recognition in practice of the present invention.

Fig. 10D is a series of steps that may be added to the data acquisition

25   and chemical recognition processes using alpha curve fitting in practice of the present invention.

Fig. 10E is a diagram of a more complex data structure that can be used in practice of the present invention.

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Fig. 10F is a sequence of processes that may be used to distinguish monomer and cluster peak responses in practice of the present invention.

Fig. 10G is a diagram of a process showing how monomer and cluster scores may be combined in practice of the present invention.

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DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

A.   A Field Asymmetric Ion Mobility Spectrometer

5   By way of general introduction, the present invention has particular
application to high field ion mobility spectrometry and includes the recognition
that improved identification or discrimination of compounds may be achieved.
However, the invention may be practiced in many different field-driven and
gas-driven embodiments.

10   One aspect of our innovation can be stated in terms of the steps of a
process. Specifically, a system is used to cause species of unknown ions to
travel through an excitation field. The field has a varying influence upon the
behavior of different ions as they travel through the field. Identification is
based on this known field-dependent behavior of different species of ions.

15   Identification of the species may occur by comparison of results observed under
one set of field conditions with results observed under another set of field
conditions.

          Various techniques may also be applied to increase the amount of, or
confidence in, the detection data and subsequent identifications. The result is

20   more accurate species detection with reduced false positives.

          Now more particularly, one device that may make use of the invention,
shown in Fig. 2, is a planar Field Asymmetric Ion Mobility Spectrometer
(FAIMS) apparatus 10. The apparatus has a sample flow section 10 that
accommodates the flow of a carrier gas G which carries sample S from sample

25   inlet 12 at one end of the flow channel 11 to a sample outlet 13 at the other end
of the flow channel.

          In operation, the sample is drawn from the environment or received from
a front end device, such as a gas chromatograph, and flows into an ionization
region 14. Compounds in the sample are ionized by an ionization source 16 as

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the sample flows through the ionization region 14, creating a set of ionized

molecules 17+, 17-, with some neutral molecules 17n, of various chemical

species that are in the sample S. This may include monomer ions and cluster

ions. Such clusters may be created when a monomer combines with water

5   molecules or other background molecules, and the combination is ionized.

The carrier gas carries the ionized sample into the ion filter region 18 in

between filter electrodes 20, 22 of ion filter 24. Filtering proceeds now based

on differences in ion mobility in the filter field, which is influenced by ion size,

shape, mass and charge.

10   More specifically, an asymmetric field applied across the filter

electrodes alternates between high and low field strength conditions in filter

region 18. The ions move in response to the field, based on their mobility

characteristics. Typically the mobility in the high field condition differs from

that of the low field condition. This mobility difference produces a net

15   transverse displacement of the ions as they travel longitudinally through the

filter 24, defining an ion trajectory.

In one example, the carrier gas (or other flow mechanism) carries the

ionized sample into the ion filter region between the filter electrodes. Filtering

proceeds based upon differences in ion mobility, which is influenced by the ion

20   size, shape, mass, and charge. This enables discrimination of ions species based

upon their mobility characteristics.

In accordance with the preferred embodiment of the present invention,

an asymmetric field voltage or dispersion voltage, variously referred to herein

as "RF", "Vrf", or "Vdisp", is applied across the filter electrodes as an RF

25   voltage driven between high and low field strength conditions. This excursion

causes the ions to move transverse to the flow as they flow through the flow

channel, with the transverse motion being representative of their characteristic

ion mobility. Typically, the mobility in the high field condition differs from

that of the low field condition. This mobility difference produces a net

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transverse displacement of the ions as they travel longitudinally through the filter between the electrodes.

The compensation voltage, Vcomp, causes a particular ion species to be returned toward the center of the flow path, thus being able to exit the filter

5   without colliding with the filter electrodes and without being neutralized. Other species will not be sufficiently compensated and will collide with the filter electrodes 20, 22 and will be neutralized. The neutralized ions are purged by the carrier gas, or by heating the flow path 11, for example.

10   B.   FAIMS Device Detecting Response Under Several Field Conditions

Therefore, in the presence of set asymmetric field conditions, as applied through Vrf and Vcomp, discrimination of ions from each other according to mobility differences can be achieved. However, in a single mobility scan, when

15   two ions are compensated by the same compensation signal in a given RF field, there is, in general, no way to discriminate between them after they pass through the filer 24. This would happen where they exhibit the same mobility characteristics for those given field conditions.

In practice of an embodiment of the present invention, however, these

20   ions can be discriminated if they have different polarities, as such is the example with ions 17- and 17+. Thus the device of Fig. 2 can be operated to simultaneously detect both positive and negative ions in the gas flow, enabling identification of two compounds simultaneously or enabling detection of two modes of a single compound simultaneously.

25   More specifically, the two species of ions 17+ and 17-, enter the detection region 25 where further separation occurs followed by their intensity determination. In a preferred embodiment, the detector 26 includes a first detector electrode 28 and a second detector electrode 30. Electrode 28 may be positively biased and therefore attracts ion 17- and repels ion 17+. Electrode 30

30   may be biased negatively, and attracts ions 17+ while repelling ions 17-. Thus,

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this final stage of separation terminates with the separated ions depositing their charges on the appropriately biased detector electrodes 28 or 30. The signals generated by the ions collecting at detector electrodes 28 and 30 are amplified by respective amplifiers 36 and 38 to provide signals to command and control

5   unit 34.

In the preferred embodiment, the invention applies to high field asymmetric waveform ion mobility spectrometry in a planar device configuration such that the flow channel 18, filter electrodes 24, and detector electrodes 28 are all provided in a planar package. This provides for the ability

10   to produce a compact, low cost device which may have incorporated upon a common substrate the various system components and possibly support electronics. Spectrometers according to the present invention may therefore be manufactured using well known microchip manufacturing techniques while at the same time providing highly effective analytical equipment for use both in

15   the field and in laboratory environments.

It is a feature of a FAIMS spectrometer that by application of compensation to the filter field, ions having specific mobility characteristics will be returned toward the center of the flow path and will pass through the filter. Therefore, in practice of the invention, discrimination of ions from each other

20   according to the compensation results in a ions having a particular mobility passing to detector 26 (which may be an on-board electrode arrangement or may include an off-board detector such as a mass spectrometer, for example). All other species will not be sufficiently compensated and will collide with the filter electrodes and will be neutralized.

25   In the preferred embodiment, the invention applies to high field asymmetric waveform ion mobility spectrometry in a planar device configuration such that the flow channel 18, filter electrodes 24, and detector electrodes 28 are all provided in a planar package. This provides for the ability to produce a compact, low cost device which may have incorporated upon a

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common substrate the various system components and possibly control electronics 40. Spectrometers according to the present invention may therefore be manufactured using well known microchip manufacturing techniques while at the same time providing a highly effective analytical equipment for use both in the field and in laboratory environments.

5

The control unit 40 contains a number of electronic devices that perform a number of important functions in accordance with the present invention. These include RF voltage generator 42, compensation voltage generator 44, a microprocessor unit (MPU) 46, memory 47, an analog-to-digital converter 48, and display 49. The microprocessor 46 provides digital control signals to the RF (AKA "dispersion") voltage generator 42 and compensation voltage generator 44 to generate the desired drive voltages for the filter 24, respectively. They may include, for example, digital-to-analog converters that are not shown in detail.

10

15

The microprocessor 46 also coordinates the application of specific dispersion voltages Vrf and compensation voltages Vcomp with observed responses from the detector 26, as read through the analog-to-digital converters 48. By comparing an observed response of, for example, peak observed abundance of a particular ion across a range of compensation voltages, Vcomp, the microprocessor 46 can identify particular compounds such as by comparing particular response curves against a library of response curves or other data stored in its memory 47. The results of the comparison operation can then be provided in a form of an appropriate output device such as a display 49, or may be provided by electrical signals through an interface 50 to other computer equipment.

20

25

One detailed example of how the microprocessor 46 can detect responses under multiple field conditions is described below in connection with Figs. 10A – 10G.

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In practice of an embodiment of the invention, a range of applied peak
RF voltages may run from less than 1,000 V/cm to 30,000 V/cm, or higher. The
frequency ranges may run from 1 to 20 Megahertz (MHz), with the highest
frequencies having an approximately 30 percent duty cycle, although other

5   operating ranges, voltages, field strengths, duty cycles, wavelengths and
frequencies are possible in embodiments of the present invention.

In practice of one embodiment of the invention, the processor 46 scans
or sweeps a range of compensation voltages (i.e., a scan) for a particular RF
field strength as controlled by the applied peak RF (dispersion) voltage for a

10   first measurement set, and then the RF is reset to another level and the
compensation voltage is scanned again to establish a second measurement set.
This information is correlated with detection signals obtained as set forth above,
and compared to look up tables, a compound identification is able to be made.

More generally stated, an object of identification is to detect the

15   intensity of the ions passing though the filter and to associate this intensity with
field conditions. Each identified compound is to be associated with at least one
particular spectral peak and then we can use the process of peak evaluation or
peak matching to identify compounds, peak by peak. This process is not limited
to single peaks and multiple peaks detected in a single scan also can be used to

20   define a signature for the responsible particular combination of compounds. If
it is a recurring phenomenon, then such complex signature can be part of our
table of look up data.

If a particular combination of peaks in a spectral scan is known and
important, data representing these multiple peaks can be stored and future

25   detection data can be compared against this stored data. For example, under
controls field conditions, such as at raised field strengths, a clustered compound
may become declustered. The resulting detection results in a signature of peaks
that can be used to identify the source compound being detected even in as
detected in a single scan.

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In practice of the invention, we have developed an ion mobility-based method and apparatus for detection of sulfur-containing compounds in a hydrocarbon background. In one example, detection and measurement of negative ions is done in a negative mode, and detection and measurement of

5   positive ions is done in a positive mode. The detected data enables a quantitative measurement of concentration of these sulfur-containing compounds, independent of the hydrocarbon background.

C.   Positive and Negative Field Measurement

10

. Referring to the illustrative embodiment of Figure 2, a single positively biased detector electrode 30 (or 28) downstream from the filter can be used to detect the negatively charged ion stream (negative mode), and optionally another other electrode 28 (or 30) may be negatively biased to deflect the

15   negative ions to the positively biased detector electrode. Also, a single negatively biased detector electrode 28 (or 30) downstream from the filter can also detect the positively charged ion stream (positive mode), and optionally the other electrode 30 (or 28) may be positively biased to deflect the positive ions to the negatively biased detector electrode.

20   Thus, positive and negative modes may be detected in the FAIMS spectrometer, seriatim or in parallel devices. Optionally, in a single scan of a single device, we are able to demonstrate simultaneous collection of multiple data by detecting both modes simultaneously. Referring again to the illustrative embodiment of Figure 2, in one example, a single positively biased electrode 30

25   downstream from the filter is used to detect the negatively charged ion stream (negative mode); meanwhile electrode 28 is negatively biased to deflect the negative ions to this positively biased detector electrode 30 so as to improve collection efficiency. However, simultaneously, if desired, the negatively

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biased electrode 28 detects the positively charged ion stream (positive mode) that is deflected by the positively charged electrode 30.

A detection signal is generated as these ions deposit their charges on a respective detector electrode. These detections can be correlated with the RF
5   signal, compensation voltage and detector bias, to definitively identify the detected ion species. Thus Where two detector electrodes are provided downstream, each oppositely biased, both positive and negatively charged ion species can be detected and identified simultaneously.

In one embodiment, the present invention was used for detection of trace
10   amounts (ppm, ppb, ppt) of mercaptan in varying and even high hydrocarbon backgrounds. The device is also able to characterize hydrocarbon gas backgrounds. For example, the present invention is capable of detecting mercaptans, such as ethyl mercaptan in a methane background, and is also capable of detecting a gas, such as methane, in a mercaptan background.

15   In this practice of the invention, where mercaptans were detected in hydrocarbon background, the asymmetric voltage applied to the ion filter electrodes ranged from about 900 to about 1.5 kV (high field condition), and a low voltage of about -400 to -500 V (low field condition). The frequency ranged 1-2 MHz and the high frequency had an approximate 30% duty cycle,
20   although other operating ranges are possible. In one embodiment, the detector electrodes were biased at +5v and -5v. Now the mercaptans are detected in the negative mode and the hydrocarbon gases can be detected in the positive mode.

The hardware used to drive the system my be conventional. For example, amplifiers, such as Analog Devices model 459 amplifier, may be used.
25   The signal may be processed in a conventional manner, such as with a National Instruments board (model 6024E) to digitize and store the scans and with software to display the results as spectra, topographic plots or graphs of ion intensity versus time. The ionization source may be a plasma or radioactive source or a UV lamp, or the like.

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The present invention recognizes that ions that pass through the filter define a mobility species 17m. In a further example, this species can be further separated by polarity, such as by correct biasing of the detector electrode pair 28, 30. An example is shown in Fig. 2 where the species defined by ions 17+,

5   17- passes through filter 24. This species can be further separated to positive and negative species or sub-species by holding one electrode, e.g., detector electrode 28, at one polarity, say negative, and another electrode, e.g., detector electrode 30, at a positive bias. Now ions 17+ will be attracted to electrode 28 and will be detected and ions 17- will be attracted to and will be detected at

10   electrode 30.

Therefore, apparatus of the invention can be operated to simultaneously detect both positive and negative ions in a species flowed from the filter. This enables identification of multiple compounds simultaneously in practice of the innovation.

15   More specifically, the apparatus 10 discriminates between ions and neutrals based on their mobility behavior, resultant trajectory and polarity. Therefore only ion species 17- and 17+ with a particular mobility behavior and resultant trajectory in the presence of a given compensation bias will be passed by the filter, for a given asymmetric RF field condition.

20   It will be appreciated by a person skilled in the art that this compensation bias must be established for the compounds being tested. The apparatus of the invention is very stable and test results are repeatable. Therefore, in a preferred practice of the invention, creation of a history table for species of ions detected, correlated with compensation voltage and RF field,

25   enables continuous use of the device without the need for further calibration. However, it is also within the scope of the invention to calibrate the system using the reactant ion peak or a dopant peak, for example.

In one practice of the invention, a mobility species 17m was passed by filter 24. That species included hydrogen sulfide ions 17m- and methane ions

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17m+, both of which have a similar resultant trajectory, for given compensated asymmetric field. Other positive and negative ions are neutralized given their different and unselected mobility characteristics. (Neutralized ions 17n are purged by the carrier gas or by heating the flow path 11, for example.)

5   The two species of ions 17m+ and 17m- have entered into the detection region 25, where further species separation occurs, followed by detection. In a preferred embodiment, detector electrode 28 is biased positive and therefore attracts hydrogen sulfide species 17m- while repelling methane species 17m+. Electrode 30 is biased negative and attracts methane species 17m+, while

10   deflecting sulfide ions 17m-. Thus this final stage of separation results in the separated ions depositing their charges on the appropriately biased detector electrodes (i.e., negative charge on positive electrode and positive charge on negative electrode).

The asymmetric field and compensation bias are generally applied to

15   filter electrodes 20, 22 by drive circuits 32 within command and control unit 34. The signals generated by the ions at the detector electrodes 28, 30 are amplified by amplifiers 36, 38, also under direction and control of unit 34 (communicating by wires, ribbon cable, or the like). A computer (or microprocessor) including a data store, generally shown at 40 correlates historical data for the device with

20   the drive signals applied to the filter electrodes and with detection signals from amplifiers 36, 38, and presents a compound identification information to a readout device 49. In this example, an indication of the amount of hydrogen sulfide and of methane detected would be indicated.

In a particular embodiment, the command and control unit 34 also

25   coordinates ion flow and the application of specific dispersion voltages Vrf and compensation voltages Vcomp with observed responses from the detector 26. By comparing an observed response of, for example, peak observed abundance of a particular ion across a range of peak RF voltages, Vcomp, the microprocessor can identify particular compounds such as by comparing

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particular response curves against a library of response curves stored in its memory. The results of the comparison operation can then be provided in a form of an appropriate output device such as at a display, or may be provided by electrical signals through an interface to other computer equipment.

5   In this embodiment of the invention, a single spectrometer device 10 provides a detector with dual detector electrodes 28, 30. One electrode may be positively biased and the other negatively. In the positive mode, the negatively biased detector electrode acts for ions of the same polarity as a deflector electrode, deflecting those ions toward the positively charged detector electrode

10   for detection. In the negative mode, the one detector electrode that is positively biased acts for ions of the same polarity as a deflector electrode, deflecting those ions toward the negatively charged detector electrode for detection. In simultaneous operation, each of these detector electrodes has a dual role, acting as both a deflector electrode and detector electrode, for respectively charged

15   ions.

          In practice of one embodiment of the invention, by sweeping the compensation bias over a predetermined voltage range, a complete spectrum for sample S can be achieved. By intelligent control of the system command and control unit 40 it is possible to select specific field conditions and as a result it is

20   possible to allow ion species of interest to pass through the filter while all other candidates are neutralized. In another embodiment, the compensation bias is in the form of varying the duty cycle of the asymmetric field, without the need for compensating bias voltage. In any such manner, the apparatus is tunable, i.e., it can be tuned to pass only desired selected mobility species, which can be further

25   clarified with the above polarity mode detections.

          In a preferred embodiment of the invention, the high voltage RF signal is applied to one filter electrode, e.g., electrode 20, and the other electrode, e.g., electrode 22, is tied to ground. A compensation voltage is then applied to one or across the filter electrodes according to the ions species to be passed. It has

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been further found that biasing the detector electrodes 28, 30, with a floating
bias, such as with electrode 28 being held at -5 volts and electrode 30 being held
at +5 volts, leads to good performance for detection of mercaptans in
hydrocarbon or air backgrounds.

5   Experimental data verifies viability of this approach. Turning now to
Figs. 3A and 3B, we show detection of ethyl mercaptan independent of varying
background gas level. Fig. 3A shows positive ion detection mode ("positive
mode") detection, where a detector electrode is negatively biased and attracts
positive methane ions 17m+ for detection. Fig. 3B shows the effect of varying

10   methane concentration on ethyl mercaptan spectra in the negative ion mode
("negative mode"). Here a detector electrode is positively biased and attracts
the negative mercaptan ions 17m- for detection.

          These spectra are for different amounts of ethyl mercaptan in an air and
methane drift gas mixture in positive mode operation and then in negative mode

15   operation of an embodiment of the invention. The mercaptan signatures are
clearly captured independent of the air-hydrocarbon drift gas background, at
various dosage levels. The detected sample peaks are fully isolated from the
background. In Fig. 3A the reactant ion peak (RIP) is clearly isolated; and in
Fig. 3B the background is flat.

20   The foregoing is an example of ionization of a particular compound(s)
that results in a combination of positive and negative ions. Both ion types can
be evaluated simultaneously in practice of an embodiment of the invention for
unambiguous identification of the test chemical. For example, a mercaptan
sample when ionized may have predominantly negative ions, but may also

25   include positive ions. Now identification can be more accurate and false
positives reduced by using both modes simultaneously to state a unique
detection signature. Specifically, while the negative mode fairly identifies the
mercaptan, the added positive ion identifier related to mercaptan enables
identification in a complex sample. The stored lookup data of known device

performance and known species signatures may be accessed for either single mode or simultaneous mode detections. By comparison with historical detection data for the device, these peaks can be clearly identified as the tell-tale spectra of the mercaptan. Both spectra give clear indication of the mercaptan,

5   qualitatively and quantitatively. Running both modes simultaneously clearly identifies the sample with unique and definitive detection data which can be compared to and matched with stored data to identify the detected ions.

Thus it will be appreciated that the present invention is capable of real-time analysis of a complex sample, such as one containing mercaptans and

10 hydrocarbon gas, because these ions are relatively of the same mobility and can pass through the filter under the same field conditions.

Simultaneous positive and negative mode detection in a single mobility scan thus provides a richness of detection data. This increased identification data results in a higher level of confidence, and reduced false positives, in

15 compound identification. This is a valuable improvement over the simple prior art FAIMS method of peak identification.

The data that can be obtained from a negative mode scan is normally different from that of a positive mode scan. While identification of a compound may be achieved by using one mode only, the used of detections from both

20 modes makes for a more definitive identification with lower likelihood of error.

D.   Improved Processing of Detection Data

The foregoing demonstrates favorably obtaining multiple detection data

25 from a single mobility scan for positive identification of detected ion species in a sample. This innovation is useful in many applications. Notwithstanding this valuable innovation, we also can obtain a still higher level of confidence, and further reduced false positives, by (1) obtaining multiple detection data from multiple mobility scans, and (2) further processing such data to extract device

30 independent attributes, such as a mobility coefficient, α.

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1.   Multiple detection data from multiple mobility scans.

In this "multiple scan" embodiment, ions are identified based on not a

5   single set of field conditions, but based on multiple intensity data detected at at

least two and possibly additional numbers of high field conditions (i.e., at at

least two field measurement points). Detections are correlated with the applied

RF voltage and compensation, at the at least two different field conditions, to

characterize a given detected compound. Because multiple detection data are

10   associated with a given ion species of interest, more accurate detections can be

made. Comparison with stored data results in reliable identification of detected

compounds.

Strategies for identification of detected ions based on data in spectral

peaks or in mobility curves include: curve matching, peak fitting, and

15   deconvolution (for overlapping peaks), and like techniques. These techniques

enable identification of detected ion species based peaks in a single scan,

including simultaneous positive and negative mode detections, and also in

multiple scans. The goal is the same: identification of multiple detection data

that can be used to definitively identify the species of a detected ion.

20   More particularly, we have observed that different ion species of

chemicals exhibit different mobility as a function of the compensated applied

RF peak voltage that generates the high field conditions. Thus, by applying a

set of different RF peak voltages and measuring the compensation voltages at

the peak locations for the various compounds, we can develop a family of

25   measurement points characteristic of a compound. This family of points can

then be plotted to determine the mobility curve signature for specific species as

a function of RF peak voltage and compensation. We can record such data and

use it for comparison and identification when future detections are made of

unknown compounds.

Furthermore, we can extract field condition data, e.g., field strength and compensation voltage for two nearby detections of the same ion species. We can then calculate the mobility curve, or at least the sign and slope of the curve between those two data points as a signature of the detected ion species. We

5 can simply store this data as the signature of that compound along with the field conditions that generated such data. In the future, when two nearby or associated peak detections are made for that species, we again know the field conditions and can compute the sign and slope, or other mathematical variables representing of the curve, for comparisons to the stored data for match and

10 identification. This approach is successful with a high degree of reliability; more complete curve matching is possible but is not required.

As will be appreciated by a person skilled in the art, the selection of measurement points and the number of measurement points may be adjusted for the specificity required for a particular application. The minimum number of

15 measurement points is two, which at least identifies an aspect (such as slope) of the characteristic curve for a compound, given the known field values.

As shown in the multiple scan data collected and recorded in Fig. 1C (prior art), each compound has a unique characteristic mobility curve that expresses the peak detection data associated with that compound at each of

20 various associated peak RF and compensation values. Thus, detection of four different chemical compounds is shown including lutidine, cyclohexane, benzene, and a chemical agent simulant dimethyl-methyl-phosphonate (DMMP). Each curve shows detection peaks at the various field conditions that is characteristic for the compound.

25 The plot of compensation voltage versus dispersion voltage (i.e., RF peak voltage) in Fig. 1C shows the associated compensation voltage for the spectral peak for each of the particular compounds illustrated at a given RF peak. As is seen from the plot, there is a region (indicated by reference numeral 100) in which the response for DMMP and cyclohexane more or less overlap

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with one another (i.e., their mobility curves overlap). Therefore, operating in a peak RF voltage region of from approximately 2,500 to 2,650 volts, at around -6 to -8 volts compensation, one would find it impossible to discriminate between the two compounds upon a single scan. In other words, the conventional

5   spectral scan would plot the overlapping peaks as a single peak at that field condition. Peak matching here would be inadequate, except for further software "tweaking" required to separate the peaks. However, this tweaking might not be matched by the stored data of a limited lookup dataset, and therefore identification could fail. This certainly is possible in a portable device that has

10   real world size, space, computing power or other limitations.

We have recognized that by taking a look at an overall response of a FAIMS system to a range of RF peak voltages, over a range of compensation voltages, for a given chemical sample, we can note that each of the curves exhibits a unique signature of field behavior. We call this mobility behavior a

15   signature mobility behavior, and can identify the compounds by this signature behavior.

It will thus be appreciated that a preferred practice of the present invention contemplates stepping the RF peak voltages and scanning the compensation voltages to generate unique sets of data that identify and

20   distinguish the detected compounds to create a data store of mobility signatures. We then have a data to store for lookup that characterizes these mobility curves and can be used for compound identification. This process will be explained in greater detail in connection with Figs. 10A-10F.

We have discovered, therefore, that identification and quantification of

25   unknown chemical species can be improved by generating, for each species, an experimentally determined curve of mobility versus applied electric fields. However, rather than comparing simply the peak observed mobility versus electrical field, mobility is determined over a range of compensated fields, possibly including relatively low voltage field strengths (where mobility may be

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the same for some compounds) and including relatively high electric field strengths (where mobility is generally different for many chemical compounds). Comparison of a spectral curve or mobility curve generated with the detected data may be made against stored curve data for positive identification.

5   Thus, by looking at a trend, i.e., the shift of the spectral peak and associated compensation voltages from the first to second field conditions, we can better confirm the identity of the compounds. In other words, other chemical compounds would not have the same combinations of shifts at the same data locations, so that accurate identification is made more likely.

10   For a generalized example, refer to Figs. 4A and 4B, showing detection intensity (abundance) as a function of compensation voltage at a particular applied field strength. Note in Fig. 4A that peaks 110-1, 110-2, 110-3, and 110-4 occur at a given Vcomp, with Vrf at 1400v (with a field strength of 28,000v/cm). Accordingly, as Vrf is changed to 1450v (field strength of 29,000

15   v/cm), shown in Fig. 4B, the set of peaks shifts to location at different Vcomp. Thus it is clear that applying even a slightly different field condition will result in peak locations being at least slightly displaced, as indicated by shifts in associated compensation level. These observations can thus be used in a process of identifying detected ion species by collecting RF and Vcomp levels

20   and correlating with detection data and then performing a comparison with stored identification data for known ions species. Upon making a match or near match, an identification of the detected species can be made.

It will now be understood that it is possible to control field conditions and to discriminate between compounds that are ordinarily difficult if not

25   impossible to separately identify by other means. Selection of field conditions enables isolation of an ion species of interest. Furthermore, because the system of the invention matches detection data with stored data, we can select field conditions that will produce detection data that is matchable to stored data, assuming the relevant ion species is present in the sample.

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Turning to Figs. 5A and 5B, we demonstrate the selectivity available in -
practice of the present invention. In Figure 5A, in a field strength of 24000
v/cm, peaks for three different isomers of xylene in a sample, p-, o-, and m-,
were detected. In Figure 5A, the peaks for p- and o- are indistinguishable while
5   the peak for m- is well defined. In order to further evaluate the sample, we
perform a second detection, shown in Figure 5B in a lower field strength of
18000 v/cm, where peaks for the three different isomers of xylene are clearly
distinguished and identifiable.

It is therefore an additional recognition of the invention that better
10   discrimination between species is not always a result of higher field conditions,
as . In fact, in this example, the p- and o- xylene isomers became
distinguishable at reduce field strength. Again, now species identification is by
table lookup, preferably of multiple detection data, and regardless of whether
based on an increasing or decreasing set of field conditions.

15   What is important to recognize here is that simply increasing the field
strength does not necessarily increase resolution as has been suggested by others
(see U.S. Patent 5,420, 424). In fact, to check for the presence of a combination
of compounds (or of isomers), or upon collection of detection data that suggests
such presence, multiple detection data may be collected and used together to
20   form a signature for the detected ions. Now comparison to stored data may
provide identification of a single species or may provide identification of a
typical grouping. For example, the detection data represented in Fig. 5A or 5B
alone are each characteristic plots of the three xylene isomers; alone these plots
enable some identification but together they enable a very high degree of
25   assurance that the three xylene isomers have been detected. Therefore, a match
to stored data for both field conditions for these isomers would provide a
reliable ion species identification with low likelihood of false positives.
Furthermore, a hand-held device that merely looks at these two or similar "data

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points" would be delivered in practice of the invention as a handy xylene detector.

In another example of the invention, we generate detection data over a range of applied field conditions. For example, in Figs. 6A and 6B we show the effect of changes in field strength on the location of detection peaks at different compensation levels for hexanone and octanone. These figures present a series of plots of the response of a FAIMS device with different applied field strengths. The curves are offset on the vertical axis, with the offset increasing as electric field strength increases. While various operating ranges are possible, as an illustration, Figs. 6A and 6B may be understood as presenting the peak RF between a low of around 620 volts (lowermost plot in each) and a high of around 1450 volts (uppermost plot in each). Several attributes are noted in this series of responses. For example, paying attention specifically to the hexanone plot of Fig. 6A, a monomer peak of 601-1 of particular interest is somewhat obscured in the lowest field strength condition. However, at the highest applied field strength, the peak 601-m corresponding to hexanone is clearly discernable from the other peaks.

Several phenomena have occurred with the increase in increasing applied field strength. First, we note that a reactant ion peak (RIP) 605-1 was relatively dominant in the low field voltage reading. However, as electric field strength is increased, the RIP 605-m shifts to the left at a more rapid rate than the monomer ion peak 601-m of interest. This is because the α parameter, of the mobility coefficient for the reactant ion species, is different than the α parameter for the monomer ion of interest.

In addition, we note that the relative amplitude of the reactant ion peaks 605 decreases markedly with the increase in the electric field. Thus, RIP 605-m is observed at much lower amplitude and well separated from the monomer peak 601-m of interest at a specific field condition. While the monomer peaks 601 also shift, they do not shift by the same amount, or even as much. Thus, by

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analyzing the compound over a range of applied field conditions, a condition
can be discovered at which the RIP 605 will shift away from, or perhaps even
shift off the scale of, other observed peak voltages. In some cases this allows
easier detection of the monomer ion peak 601 of interest.

5   Similar behavior is observed in the monomer peaks 610-1, 610-..., 610-
n observed for octanone and the resulting reactant ion peaks 615-1 to 615-m.
This information can thus be used to identify a species by comparing a family of
response curves to a stored family of known response curves.

       Another observed effect in both Figs. 6A and 6B is that a so-called

10   group of cluster ions 608, 610 are seen. The cluster ions 608 represent clusters
of chemical materials in the sample. Typical cluster ions, having a heavier
chemical weight, have peaks that are shifted differently from monomer ion
peaks of interest. In particular, given that they are heavier, the cluster peaks
shift differently. In this example, the cluster peaks shift in a direction away

15   from the direction of shift of the monomer peaks with increasing applied field
strength. This characteristic feature of cluster ions observed with this sample
can also be stored and utilized in recognizing the hexanone or octonone ions.

       These curves shown in Figs. 6A and 6B are but one example of how
applying a range of field conditions to detect a given sample can be utilized to

20   advantage. Another effect can be observed with the application of relatively
high field strengths. Specifically, complex ion groupings can be fragmented
with higher field strength so that the components of the group themselves can be
individually detected.

       For example, Sulfur hexafluoride (SF6) can be very well detected in the

25   negative mode. However, the response in the positive mode, while alone not
definitive, has a profile and thus in combination with the negative mode is
confirmative and provides a lower likelihood of false detections. We therefore
can detect SF6 in the single mode of dual mode, seriatim or simultaneously.

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SF6 gas is used in atmospheric tracer applications to monitor air flow, as a tracer for leak detection in pipes to point detect sources of leaks, in power plants to isolate switches to reduce, or prevent breakdown of the switches, among other uses. Isolation and detection of SF6 is often found to be a difficult

5   proposition.

In practice of the present invention, it is possible to detect SF6 in air, getting a very distinct peak for the SF6 separate from the reactant ion peak. The reactant ion peak is composed of the ionized nitrogen and water molecules in the air.

10   In conventional IMS (time of flight) the reactant ion peak overlaps the SF6 peak. In practice of the present FAIMS innovation, in the negative ion mode (i.e., detecting negative ions passing though the FAIMS filter based on RF and compensation as shown in examples below), it is possible to clearly separate between the SF6 peak and the reactant ion peak (RIP). This success in

15   the negative mode separation between SF6 and the RIP peaks is clearly shown in Fig. 3C. However, in the positive ion mode, there is no detected difference between the signal without the SF6 present and with the SF6, as shown in Fig. 3D.

In Fig. 3E, there is a plot of the FAIMS response at different RF voltage

20   levels in the negative ion mode. Fig. 3F shows this result and also shows the RIP detected in absence of SF6. Thus clear vitality of the FAIMS filter of the invention with appropriate selection of RF and compensation voltages is shown. In both cases the SF6 peak is shifted from and distinct from the RIP.

Fig. 3G shows that FAIMS response in the positive ion mode (detecting

25   positive ions passing through the FAIMS ion filter), where the SF6 peak is not isolated from the RIP. While alone this is not definitive, it is an expected detection and therefore may be used as confirmative when combined with a definitive SF6 negative mode detection.

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In one embodiment of the invention a portable battery powered unit for - the detection of SF6 with a sensitivity of 1x10-9 atm cc/sec SF6 (0.01 PPM) is enabled. In this embodiment, the invention may be used, for example, in the power industry to ensure the leak tightness of High Voltage Switchgear and in

5   the laboratory for testing fume hoods to the ASHREA 110 specification. Other applications include torpedo head, pipework systems, and air bag integrity testing. The high sensitivity, rugged design and ease of use and set up of the invention are advantageous for many applications that involve the detection of SF6.

10   Fig. 7 is an example of such an affect on a mercaptan ion sample. In particular, a range of background voltages (from 620 – 1450 volts) were applied to an ethyl mercaptan spectra in which we see a general shift of ion peak behavior as an electric field conditions are strengthened. However, we also observe a fragmentation condition. Specifically, at lower applied field

15   conditions, strong single peak is observed, such as at 701-1. However, as electric field strength is increased, multiple peaks 701-n, 702, ... 710 are observed in a spectra. By observing and recording the peak locations not only at the low volt field conditions, but also at a range of field conditions, this fragmentation behavior can be further exploited to better identify compounds.

20   We can store data indicating the peak RF voltage at which fragmentation occurs, or the locations of the fragment peaks, and then further use it when matching detection data.

We have also been able to discover species identification method that is device-independent. Turning now to Figs. 8A and 8B, we have plotted

25   experimental detection data recorded in Table 1 (Fig. 8C) for a homologous group of ketones, including: acetone, butanone, pentanone, hexanone, heptanone, octanone, nonanone, decanone (8A- monomers, 8B- clusters). Each species has a unique mobility curve, and thus a unique mobility signature, for the given set of field conditions. We can store this data and then use the same

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device as a detector for ketones. We obtain a set of detection data and perform curve matching versus the stored data or other data comparison. A match enables identification of the detected ketone in that device. We also can take any two sets of points and store curve data, such as slope and sign, for the

5   experimentally detected data for a known species. Now with two detections, such as at peak RF field strengths (E) of 28000 and 29000 v/cm, we have two data points, between which we can compute slope and sign for a purported connecting curve function, and then we compare to stored data to make a positive identification of a detected species in that device.

10 ·   However, we can go a step further by making the identification process device-independent. Thus we create data that can be used in any system that detects field mobility dependence of an ion. This is based on determining the parameters of a function derived from the fundamental mobility coefficient associated with each species.

15   Therefore, for example, the multiple data represented in Figs. 4A and 4B and 5A and 5B each can be used to provide positive identification of a detected species by the unique and inherent mobility characteristic that identifies that species. We make this comparison to a lookup table that can be specific to the device in question, but also can be a universal set of data that is device-

20 ·   independent. Thus, in general, one does not wish to only compare the plot of abundance curves versus compensation voltage individually, but rather generate a plot of observed peak locations for specific compensation voltages, so that curves, slopes, signs, and various details can be discerned for each of the detected ions for comparison to a library of lookup data.

25

2.   Alpha coefficient determination

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More specifically, in computing mobility signatures, we have found that an expression of the field-dependence of ion mobility, the so-called α coefficient, expressed as a function of field, can be used to generate a unique α function that is inherent for that species and is device independent. Thus the α

5   function can be used as the unique signature of a species; quite remarkably, this function expresses both a characteristic signature for the ion species and is device independent. In short, we recognize that peaks change position in signature ways because they have different alpha signatures.

Thus we use the α function as a mobility signature for detected species.

10   The signature can be determined for a detected unknown compound based on the field conditions that are used, and then this can be used to make an identification according to a lookup table of stored known signature data associated with known compounds. More particularly, in practice of a preferred embodiment of the invention, ion species are identified based on the mobility

15   dependence of the species under various field conditions. Data is collected for the sample under test for at least two field conditions, the data is processed, and a comparison of detection data computed as an α function for the sample under test versus the stored data enables identification of the compounds in the sample.

20   Referring again to the discussion of the α parameter, Fig. 1B is a plot of mobility versus electric field strength for three examples of ions, with field dependent mobility (expressed as the coefficient of high field mobility, α) shown for species at α greater, equal to and less than zero. For any given set of field conditions, the field strength and compensation can be correlated with an α

25   value. This is shown in the work of Buryakov et. al., *A New Method Of Separation Of Multi-Atomic Ions By Mobility At Atmospheric Pressure Using A High-Frequency Amplitude Asymmetric Strong Electric Field, Intl J. MassSpec and Ion Proc. (1993), at p. 145.*

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We have observed that knowing the α parameter alone at a particular

field strength does not prevent false positives. This would occur at the

intersection of the two plots in Fig. 1C, at the point indicated by reference

numeral 100. Without more information, knowledge of the α parameter for the

5   respective ion species at that location does not provide unique mobility

signatures for both compounds. Thus, without doing more, any number of

readings at this intersection is likely to result in a detection error.

However, we have also found that we can express an ion's α mobility

characteristic as a function of field, i.e., as $\alpha(E)$, and can define a unique

10   mobility signature for the ion species which is device-independent. This $\alpha(E)$ or

"alpha function" relates the size, effective cross-section, shape, and mass of the

ion to field conditions. It is understood that as the applied electric field ·

increases, the increasing electric field tends to displace, stretch, and/or breaks

the bonds of the ion such that the stronger the field, the greater the induced

15   dipole, quadripole, or higher order moments of the ion. These, in turn, affect

the relative mobility of the specific ion. The result of relating these aspects is to

define a unique mobility signature for the ion species of interest. This also turns

out to be device-independent.

The relationship of the $\alpha(E)$ function to field conditions is shown in the

20   following:

$$V_c(E) = \frac{<\alpha E, f(t)>}{1 + <\alpha> + <\frac{d\alpha}{dE} E, f(t)>} \qquad (1)$$

25   where: Vc-compensation voltage (peak position); Es-electric field strength; f(t)-

waveform parameters (waveshape and so forth).

Thus for each spectral detection, we can compute α as a function of field

conditions, i.e., $\alpha(E)$. Specifically, the asymmetric waveform in a planar field

asymmetric waveform mobility spectrometer, $E_{max}(t) = E_{max}f(t)$, is designed to satisfy the following conditions:

$$1/T \int_0^T E_s(t)dt = <E_s f(t)> = 0 \qquad (3a)$$

$$<f^{2n+1}(t)> \neq 0 \qquad (3b)$$

5   where $f(t)$ – is a normalized function which describes the waveform, and E_{max} is the maximum amplitude of the waveform. The waveform is designed such that its average value is zero (equation 3a) while the polarity of the electric field during one period is both positive and negative. The addition of the compensation field, C, to the waveform $E_s(t)$ yields Equation 4:

$$E(t) = E_s(t) + C = E_s f(t) + C \qquad (4)$$

10   so the average ion velocity over a period of the asymmetric waveform can be written as:

$$V = <V(t)> = <K(E)E(t)> \qquad (5)$$

Only ions with average velocity of zero, v = 0, will pass through the gap without neutralization. An expression for the compensation field required to enable an ion to pass through the gap can be obtained by substituting Equations

15   2, 3, and 4 into Equation 5 as shown in Equation 6:

$$C = \frac{<\alpha E_s f(t)>}{1 + <\alpha.> + <\frac{d\alpha}{dE} E_s f(t)>}. \qquad (6)$$

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The value of this compensation electric field can be predicted precisely when the alpha parameter for the ion species, the waveform $f(t)$, and the amplitude of the asymmetric waveform E_{max} are known.

A procedure for extraction of $\alpha(E)$ from experimental measurements of the electric field dependence of the mobility scans is thus known. In this section, some additional considerations regarding the alpha parameter and methods to determine this parameter described. First, emphasis must be given that the alpha parameter is a function (not a number) and the physical and chemical information about an ion is contained in the shape of the $\alpha(E)$ curve. The method of representing this curve is incidental to the topic. The only criterion critical in these methods is that the calculated values for mobility (i.e. $K(E) = K_o\{1+\alpha(E)]\}$) should be as close as possible to the experimental values. The function for $\alpha(E)$ can be represented as an even power series or in complex form. In either instance, the curves of experimental results and calculated should agree closely. Thus, the quality of the approximation is limited by the accuracy of the experimental results and has been illustrated. Discerning the quality of a model based upon two parameters, three parameters, or a nonlinear function with five parameters was difficult. All approximations were located within the error of ΔC_1 (at $\pm 9\%$).

In this work, a simple uniform method is described to represent the function of $\alpha(E)$, which will be suitable for comparison of results obtained under different experimental conditions. These methods could be used for differing asymmetric waveforms or different designs of IMS drift tubes: linear, cylindrical, or planar FAIMS. In general then, the criteria for choosing the level of approximation of alpha is first to ensure that the method of extracting the alpha parameter uses the least number of individual parameters of the experimental device. Second, the result should contain the fewest number of adjustable parameters, and the approximation curves should be within the

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experimental error bars. In the next section, the general method to extract the alpha parameter is described and then applied in the subsequent section.

The function of $\alpha(E)$ can be given as a polynomial expansion into a series of electric field strength E degrees as shown in Equation 7:

$$\alpha(E) = \sum_{n=1}^{\infty} \alpha_{2n} \cdot E^{2n} \qquad (7)$$

5   Substituting Equation 7 into Equation 6 provides a value of the compensation voltage as shown in Equation 8 where an uneven polynomial function is divided by an even polynomial function. Therefore an odd degree polynomial is placed after the identity sign to approximate experimental results:

$$ (8) $$

$$ C = \frac{\displaystyle\sum_{n=1}^{\infty} \alpha_{2n} S^{2n+1} \langle f^{2n+1}(t) \rangle}{1 + \displaystyle\sum_{n=1}^{\infty} (2n+1)\alpha_{2n} S^{2n} \langle f^{2n}(t) \rangle} \equiv \sum_{n=1}^{\infty} c_{2n+1} S^{2n+1} \langle f^{2n+1} \rangle $$

This allows the a comparison of the expected coefficient (approximated) to be
10   compared to the values of alpha parameter as shown in Equation 9:

$$ c_{2n+1} = \alpha_{2n} \langle f^{2n+1} \rangle - \sum_{k=1}^{n-1} (2(n-k)+1) c_{2k+1} \alpha_{2(n-k)} \langle f^{2(n-k)} \rangle \qquad (9) $$

Alternatively, alpha parameters can be calculated by inverting the formula by using an approximation of the experimental results per Equation 10:

$$ \alpha_{2n} = \frac{1}{\langle f^{2n+1} \rangle} \{ c_{2n+1} + \sum_{k=1}^{n-1} (2(n-k)+1) c_{2k+1} \alpha_{2(n-k)} \langle f^{2(n-k)} \rangle \} \qquad (10) $$

Any number of polynomial terms (say 2n), in principle, can be determined from Equation 10 though a practical limit exists as the number of polynomial terms in
15   the experimental result of the approximation c_{2n+1} should be higher than the expected number of alpha coefficients α_{2n}. Since the size of n depends on the experimental error, the power of the approximation of the experimental curves $C(E_s)$ cannot be increased without limit. Usually N experimental points of

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$C_i(E_{si})$ exist for the same ion species and experimental data can be approximated by the polynomial using a conventional least-square method. Finally, the number series terms cannot exceed the number of experimental points so increasing the number of series terms above the point where the fitted curves are

5   located within the experimental error bars in unreasonable. In practice, two or three terms are sufficient to provide a good approximation shown in prior findings. The error in measurements must be determined in order to gauge the order of a polynomial for alpha. The sources of error in these experiments (with known on estimated error) were:

10   1. Error associated with measurement and modeling of the RF-field amplitude ($\sim$5%);

2. Error in $C(E_s)$ from a first-order approximation of Equation 4 ($\sim$3%), and

3. Error in measuring the compensation voltage ($\sim$5-8%).

An approximate error may be $\sim$10% and there is no gain with approximations

15   beyond two polynomial terms; thus, alpha can be expressed as

$\alpha(E/N) = 1 + \alpha_1 (E/N)^2 + \alpha_2 (E/N)^4$ with a level of accuracy as good as permitted by the measurements.

A standard least-square method (regression analysis) was used to approximate or model the experimental findings. For N experimental points

20   with $C_i(E_{si})$ and for $C = c_3 S^3 + c_5 S^5$ a function $y = c_3 + c_5 x$ can be defined where $y = C/S^3$; $x = S^2$ so c_5 and c_3 are given by Equations 11 and 12, respectively:

$$c_5 = \frac{\sum_{i=1}^{N} x_i \sum_{i=1}^{N} y_i - N \sum_{i=1}^{N} x_i y_i}{\left(\sum_{i=1}^{N} x_i \right)^2 - N \sum_{i=1}^{N} x_i} \qquad (11)$$

$$c_3 = \frac{1}{N} \left(\sum_{i=1}^{N} y_i - c_5 \sum_{i=1}^{N} x_i \right) \qquad (12)$$

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Through substituting experimental value c_3, c_5, values for α_2 and α_4 can be found per Equations 13 and 14:

$$\alpha_2 = c_3 \Big/ \langle f^3 \rangle \tag{13}$$

$$\alpha_4 = \frac{c_5 + 3c_3\alpha_2\langle f^2 \rangle}{\langle f^5 \rangle} \tag{14}$$

In order to calculate α_{2n}, knowledge is needed for the approximations of

5   experimental curves for $C(E_s)$ and for the function $f(t)$ – which is a normalized function describing the asymmetric waveform.

For example, nine data points were identified for each of the eight ketones of Fig. 8, based on the data collected in Table 1 of Fig. 8C. These can

10 be used to compute the α curve for that species, such as with a piecewise linear approximation to the α curve. For example, two data points for butanone are a(Vcomp-a, Vrf-a) and b(Vcomp-b, Vrf-b). Between these two points, the slope and sign of the butanone curve can be computed. More complete characterization of the curve, such as with polynomial curve fitting, is also

15 possible.

Now this data set becomes part of a data store for use in identification of the species of an unknown detected ion species for which two data points are collected and the corresponding curve data is computed. In short, in a simple practice of the invention, we collect data on at least two closely associated

20 points (peaks) for a given ion sample and generate the curve data accordingly. Once we have the detected and computed data, we assume this approximates the alpha curve and therefore do a lookup to our stored data. Upon finding a match, we can then positively identify the sample.

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In Fig. 9A and 9B (monomers and clusters, respectively) we computed unique α curves for ketone ions (acetone, butanone, pentanone, hexanone, heptanone, octanone, nonanone, decanone) based on data collected in the Fig. 7B Table, plotting the percent change in α against the change of field strength

5   for the various data collected ion Table 1 (Fig. 8C). These plots of percent change in α against field strength express a unique signature for each of these ion species. This is loaded in our data store for later comparison: the signature data includes the RF field strength and the compensation voltage at which the peak is detected, we also associate with it the identifying data for the known α

10   function associated with that detected peak location and field conditions for each species.

Figs. 9A and 9B thus express the α function for individual ketones spanning electric fields of 0 to 80 Td (~23 kV/cm), expressed as a percentage change in alpha as a function of field conditions. These plots are fundamental

15   signature features of these ion species that are independent of the drift tube parameters and can be used in other mobility spectrometers. Thus the α function can be favorably used in practice of the invention to provide a mobility identification data set that is device-independent.

These results are surprising and demonstrate that for chemicals with the

20   same functional group, protonated monomers of a single type exhibit a broad range of behavior vis-à-vis the dependence of coefficients of mobility on electric fields. This difference in behavior for a common moiety suggests that the effect from the electric field must be associated with other aspects of molecular structure. One possible interpretation is that ions are heated during

25   the high field and the effect on the protonated monomer should be striking. These ions with structures of $(H_3O)^+ M (H_2O)_n$ or perhaps $(H_3O)^+ M$ $(H_2O)_n(N_2)_2$, should be prone to dissociations with slight increases in ion temperature caused by the high field conditions. Thus, ion cross-sections and mobilities would accompany declustered small ions at high fields.

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Referring again to Fig. 9A, it will be noted that there is approximately a 20% increase in $\alpha(E)$ for the protonated monomer of acetone with high fields. As the molecular weight of the ketone is increased, ion heating should be less pronounced and reflected in the $\alpha(E)$ function. The $\alpha(E)$ function for proton

5   bound dimers (clusters) is consistent with decreases in mobility under high field conditions. Consequently, the basis for the $\alpha(E)$ function differs from that of protonated monomers. Indeed, the proton bound dimer for decanone undergoes a 5% decrease at high fields. The cause for a decrease in mobility at high fields has no existing model but should be due to increased collisional size or

10   increased strength of interaction between the ion and the supporting gas.

Furthermore, if we were to do the same for the cyclohexane and DMMP in Fig. 1C, the computed alpha curves would differ accordingly. In this manner, we can distinguish ion species even when their mobility curves overlap, as long as we have at least a second detection data set to associate with each detected

15   species in question. Therefore we achieve a high level of assurance for the accuracy of our identifications.

Thus we have shown that the fundamental dependence of mobility for ions in high electric field can be obtained from field asymmetric ion mobility spectrometry. Functions of dependence can be extracted from experiments

20   using known methods to treat imperfect waveforms. These findings show an internal consistency with a homologous series of ketones, and also indicates a mass dependence not previously reported.

Now it will be appreciated that in practice of the invention, ion species are identified based on ion mobility dependence of the species under various

25   field conditions. First, characteristic changes in ion mobility, based on changes in field strength and field compensation, are recorded and stored for a library of known compounds; secondly data is collected for the sample under test for a variety of field conditions; thirdly, a comparison of detection data for the sample under test versus the stored data enables identification of the compounds

in the sample. The quality of stored data and strength of the mobility relationship enables improved species identification.

It should be furthermore understood that the invention is applicable not only to planar field asymmetric ion mobility systems but may be applied in
5 general to ion mobility spectrometry devices of various types, including various geometries, ionization arrangements, detector arrangements, and the like, and brings new uses and improved results even as to structures which are all well known in the art. Thus the present invention is not limited to planar configurations of the examples and may be practiced in any other
10 configurations, including radial and cylindrical FAIMS devices. Furthermore, in practice of an embodiment of the invention, the output of the FAIMS filter may be detected off board of the apparatus, such as in a mass spectrometer or other detector, and still remains within the spirit and scope of the present invention.

15 The foregoing discussion has been focused on detection and identification of species of ions. However, this invention is broader and can be applied to any system for identification of unknown species of ions traveling through a varying controlled excitation field, the identification being based on the known characteristic travel behavior of the species under the varying field
20 conditions. The ion or ions to be identified may be traveling alone or in a group of ions of same or differing characteristic travel behavior. The field may be compensated in any of various manners as long as a species of interest is returned to the center of the flow and permitted to pass through the filter while all other species are retarded or neutralized. Identification is made based on
25 known field-dependent differential mobility behavior of at least one species of ions traveling in the field at known field conditions.

E.   A Process for Identification of Compounds

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Focusing attention now on Figs. 10A-10F a specific sequence of steps will be described that may be carried out to perform species identification in several of the embodiments of the present invention, which are provided by way

5   of illustration and not limitation. In this illustration, the sequence of steps would be performed by the microprocessor 46 which is associated with the ion mobility spectrometer device 10. As was already described in connection with Fig. 2 there would also be an RF voltage generator 42, compensation voltage generator 44, a memory 47 and an analog to digital converter 48. The

10   microprocessor 46 provides digital control signals to the RF dispersion voltage generator 42 and compensation voltage generator 44 to control the desire drive voltages for the filter 24. These may also include for example, digital to analog converters that are not shown in detail in the drawings here.

The microprocessor 46 coordinates the application of specific RF

15   dispersion voltages Vrf and compensation voltages Vcomp also taking into account the function of observing responses from the detector 26 as read through the analog to digital converter 48. By detecting attributes (such as the peaks) of observed abundances of a particular ion species across a range of Vrf voltages, the microprocessor 46 can thus take steps to identify particular

20   compounds. These may include, for example, comparing or correlating particular "response curve" data against a library of response curve data as stored in the memory 47. They can also include computation of α curve parameters. The results of the comparison operation can be provided in the form of an appropriate output device such as a display or personal computer or

25   the like, or maybe provided by electrical signals through an interface to other data processing equipment.

As shown more particularly in Fig. 10A, a state 1000 is entered into the microprocessor 46 in which a compound is to be analyzed. Here, the compound is known and identified, such as by a user supplying an identifying text string to

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the computer. A sequence of steps is then performed by which data is to be
acquired concerning the known chemical compound. From this state 1000 a
next state 1002 is thus entered in which a range of dispersion voltages Vrf and
compensation voltages Vcomp are determined by the processor 46. These

5   ranges include a beginning voltage (b) and an end voltage (s) and step voltage(s)
to be applied to each of the ranges Vrf is thus varied from an initial value Vrf(b)
to a final value Vrf(e) by a step amount Vrf(s). Similarly, Vcomp is to be
varied from Vcomp(b) to a final value Vcomp(e) by a step amount Vcomp(s).

The voltage ranges are then applied in the following steps. Specifically,

10   step 1004 is entered in which the Vrf is allowed to step through a range of
values. A state 1008 is entered next in which the compensation voltage Vcomp
is also swept or stepped through a series of values or ranges.

In state 1010 the response to each applied voltage is stored as a value, a.

If the last compensation voltage has not yet been tested then processing

15   returns to state 1008 in which the next compensation voltage is applied.
However, in state 1012 if all of the compensation voltages have been applied
then processing proceeds to a state 1014 wherein a test is made to see if all of
the dispersion have been applied.

The loop continues until all of the compensation and dispersion voltages

20   have been applied resulting set of data is then analyzed in a state 1018 to
identify features of interest. In a specific example being described it will be the
peak locations that are of interest. For each such peak in an observed response
for a given applied dispersion voltage Vrf, a response value for a specific
Vcomp is determined and its corresponding amplitude, a, is detected and stored.

25   The response curve data, or certain attributes thereof such as the peak
locations are then stored as a data object P (or table) as shown in Fig. 10B.
Such an object will typically contain an identification of the tested compound
such a text string. Also stored of course are a set of the applied dispersion
voltages Vrf. For each such dispersion voltage Vrf a corresponding peak

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compensation voltage is stored. Specifically, what is stored is at least the compensation voltage Vcomp at which a peak was observed, and typically the corresponding amplitude of the response (abundance) observed at that peak.

It is by now understood by the reader that for a given RF voltage Vrf

5   there may actually be a set of compensation voltages at which a number of "peaks" are observed. For example, as was described in connection with Figs. 6A the sample analyzed was made up of a compound of specific ions monomers, cluster ion, and reactant ion peaks. Thus, there should be an accommodation in the structure of object P to anticipate that there will be more

10   than one peak observed in any particular mobility scan, and that the number of peaks per response curve will not always be the same number.

An example data element of object P is thus shown where for a single RF dispersion voltage, Vrf-1, peaks were observed at compensation voltages Vcl1, ..., Vcln having corresponding amplitudes al1, ..., aln. Thus might

15   correspond to the case of the lowest applied dispersion voltage in Fig. 6A, where numerous peaks 601-, 605-1, 608-1 are detected. However, at another dispersion voltage Vrf-m, only a single peak at Vcomp-m, am was detected. This might correspond to a case such as in the uppermost curve of Fig. 6A, where only a single peak 601-m was detected.

20   In a typical application, a library of data objects P (reference vectors) would be developed by running the steps of Fig. 10A for different known compounds.

This would then permit an instrument to eventually enter a chemical recognition state 1200 as shown in Fig. 10C. From this state a series of

25   measurements are taken in states 1202-1214 that are not unlike the measurements taken in Fig. 10A. Specifically, a series of measurements are taken for a specified compensation and RF voltages. It should be understood that an entire set of all of the same measurements need not be taken in this mode as were taken in the chemical data acquisition mode. Specifically, not all points

-55-

on a relatively dense response curve need to be taken, only enough to identify - each compound.

　　　　Once the measurements are taken a state 1220 is entered in which features such as peaks of the response are identified for each peak a

5　　corresponding compensation voltage and amplitude may be identified and these stored to a candidate measurement vector P'.

　　　　The candidate vector P' thus represents a series of data that need to be tested against a number of candidate compounds. The candidate vector P' is then analyzed in states 1230 and/or 1240 by looking up corresponding

10　counterparts in the library of reference vector objects P, and scoring a match between P and P'. These steps may be iterated until such time as a match or a best match is determined in a state 1250.

　　　　It should be understood that any number of techniques may be used to determine a degree of match between P and P'. For example, if the elements

15　(Vcomp, a) of P and P' are considered to be data points in Euclidian geometry space, a distance can be computed. The comparison with the smallest Euclidian distance can then be selected as the best match. However, other recognition techniques may be used or to determine an identify of an unknown compound, for example, are there more sophisticated signal processing techniques such as

20　correlation may be used to resolve peaks; or other known pattern recognition algorithms, neural networks or artificial intelligence techniques may be used to find a best match for P'.

　　　　This best match is then identified to a user such as by looking up the compound identifier field and displaying in state 1260.

25　　　　Fig. 10D shows a series of steps that may be added to the data acquisition phase and the chemical recognition phase to take advantage of second order data processing characteristics. For example, in the data acquisition state, a series of states 1020, 1022, 1024 and 1026 may be added which attempt to curve-fit specific attributes of the measured response.

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Specifically, a state 1020 may be entered in which for each data element of the object P a vector, z, is formed consisting of the peak compensation voltages $vcl1$, $vcl2$,...$vclm$.

This vector is in fact a vector of point locations for the peaks observed
5   for a range of compensation voltages. Returning attention to Fig, 6A, briefly, this may correspond to for example locating the points 601-1,...601-m,...601-n corresponding to peak height and locations for the monomer ions of interest. A curve may then be fit through these peaks such as by applying a curve fitting algorithm, in state 1024. In the illustrated example it is assumed that a
10   quadratic equation is fitting the peaks of the form $y^2 = \beta x^2 + \gamma$. The β and γ coefficients can then be stored in the state 1026 associated with the vector. The chemical is thus identified by a curve fit to its peak locations approximating its mobility (α coefficient) behavior.

If this is done, a corresponding set of steps 1270, 1272 and 1274 would
15   be typically added to the chemical recognition process. Thus, peaks would be identified instead of comparing raw data values in states 1270 and 1272 by performing a curve fit to observe data and then determining γ and β coefficients. In state 1274 the β and γ coefficients would be tested to determine closest matches in the P object library.

20   Fig. 10F shows a series of steps that may be used to identify or distinguish peaks in the acquisition phase. Here initial data may be added to the objects P by identifying peaks as a cluster peak or monomer peak. Specifically, if a peak shift is observed as a range as a range of field condition voltages (e.g., Fog. 6A) is increased then this might be identified as a cluster peak. If the peak
25   does not meet specific shifting criteria it might be identified as a monomer peak. States 1310, 1331, and 132 could thus be added to the identification process. The results of these steps would add an additional parameter L associated with each data point in the object P to further identify each peak as a monomer cluster or other peak type, as shown in Fig. 10E.

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Other approaches to this could potentially be used to label peaks. For example reactant ion peaks could also be identified by running an analysis on a response of the instrument when no sample is applied. In this mode only the reactant ion peaks would occur in their behavior across a range of compensation

5   voltages could be stored. In any event, information concerning the particular type of peak can thus be stored in the pointer data in a state 1320 at which such a peak is detected. This information can then be added to the objects P specifically as shown in Fig. 10E.

Fig. 10G shows additional processing steps that might be performed in

10   the chemical recognition state to take advantage of the situation of Figure 8A and 8B in which monomer and cluster ion behavior is observed. Specifically, these steps in Figure 10G might be added as further steps 1280 in the recognition phase. Here for every candidate peak P' corresponding monomer peak in the reference array P is compared. A score is then associated with the

15   closest of the match in state 1284 similarly in state 1286 a cluster peak may be compared with its corresponding in the peak library P. A score sc is then determined in step 1288 depending on the closest of this match. Finally, in a state 1290 a final score sf can be associated with weighting the monomer peak score and the cluster peak score by weighting factors wm and wc for example in

20   an instance where cluster peaks are expected to provide more information than monomer peaks, cluster peaks might be weighted highly and monomer peaks relatively low or zero factor. This weighting is understood now how both monomer and cluster peak identification can be combined to further refine compound identification.

25   It will be evident to one skilled in the art that various modifications and variations may be made to the present invention without departing from the spirit and scope herein. For example, although illustrated in Fig. 2 was a single filter 24 and detector 28, it should be understood that a series of filters 24 can be applied to a specific gas ionized sample S. The first can be used as a pre-filter

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to limit chemical species to a particular range of species that are know to be of
interest, with the second filter in the series being used to provide for detailed
sweeping at precise incrementing voltages to provide for greater resolution.

Various illustrative examples of novel detection strategies in practice of

5 embodiments of the invention are disclosed herein. This discussion may be
applied to ions, particles, articles, biologicals, vehicles, people, things, or the
like, and variations thereof; these also may be described by alternative terms,
such as "ions", without limitation, and yet such breadth will be understood to be
within the spirit and scope of the present invention.

10 While this invention has been particularly shown and described with
references to preferred embodiments thereof, it will be understood by those
skilled in the art that various changes in form and details may be made therein
without departing from the scope of the invention encompassed by the appended
claims.

15

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CLAIMS

What is claimed is:

5   1.   A method for identification of a species of at least one unknown item
             traveling through an excitation field, the field having varying influence
             upon behavior of items traveling through the field, the method
             comprising the steps of:
                     generating a varying excitation field;
10   subjecting at least one item to the field, the item having field-
             dependent mobility that reflects field conditions;
                     subjecting the at least one item to at least two different field
             conditions in the field;
                     compensating the field conditions to pass the item through the
15   field; and
                     identifying the item as a member of a known species, the
             identification being based on known field-dependent behavior of that
             known species in those compensated field conditions.

20   2.   A method as in claim 1 further comprising the steps of:
                     defining a data store, the store including (i) data identifying a
             known asymmetric excitation field operating at known field conditions,
             (ii) data identifying a known species of items, the known species of
             items being defined by items having in common a known field-
25   dependent mobility behavior when traveling in the field at those known
             field conditions, and (iii) multiple data representing passage through the
             field of at least one item of the known species of items, the passage
             being correlated with the known field conditions;

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subjecting a sample of at least one unknown species of item to the field at selected known field conditions;

generating multiple sets of detection data that associate detection of an item of the unknown species and the passing of the item through the field at the selected known field conditions;

comparing the detection data with the data store; and

identifying the unknown species upon finding a closest match of the detection data with the data in the data store.

3. A method as in claim 2 wherein the step of generating multiple sets of detection data associated with the unknown species includes the steps of scanning the field at known field conditions, detecting negative and positive scan spectra, and processing these spectra as the multiple sets of detection data.

4. A method as in claim 2 wherein several items to be identified travel in a group of items of differing characteristic behavior, further including generating multiple data sets for multiple species, generating representative curves therefrom, and matching curve characteristics to data in the data store for identification of multiple items from multiple species in the sample.

5. A method as in claim 2 further comprising the step of calculating the coefficient of field-dependent mobility for the detected at least one item and further identifying said item by comparison of said calculated alpha data with alpha data in said data store associated with a known species.

6. A method as in claim 5 further comprising the step of calculating the sign and slope of an alpha curve associated with said alpha data for the

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detected item for identification of the species of the detected item
compared to said alpha data in said store associated with a known
species.

5   7.   A method as in claim 2 wherein the step of generating multiple sets of
detection data associated with the unknown species additionally
comprises:
collecting detection data for at least two different sets of field
conditions;
10   obtaining at least two sets of detection data associated therewith;
comparing the sets of detection data with the data store; and
identifying the unknown species upon finding a closest match for
both of the multiple sets of detection data with a single known species
defined in the data store.

15

8.   A method as in claim 1 wherein the item to be identified may be
traveling alone or in a group of items of same or differing characteristic
behavior.

20   9.   A method as in claim 1 wherein the item is an ion and the field is a
periodic asymmetric high strength electric field varying between high
and low field conditions, and the system is an ion filter system.

10.   A method as in claim 1 additionally comprising:
25   applying an excitation field of sufficient strength to fragment the
ion species.

11.   A method as in claim 10 wherein the fragmenting produces positive and
negative ions.

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12.   A method as in claim 11 further comprising identifying the positive and negative ions over the range of compensation voltages.

5   13.   A method as in claim 10 further comprising varying the electric field to produce ionized monomers.

14.   A method as in claim 10 wherein the field conditions are varied over a range of dispersion voltages to produce multiple attributes of the field

10   dependent behavior dependent on the compensation voltage.

15.   A method as in claim 14 wherein the attributes are peaks, and each peak identifies a particular ion.

15   16.   A method as in claim 1 additionally comprising the step of:
                determining a systematic function of alpha parameters for a
        homologous chemical series of compounds.

17.   A method as in claim 16 additionally comprising:

20   extracting values for α_n from trends in compensation voltage for
        an item as electric field strength is varied.

18.   A method as in claim 1 additionally comprising:
                determining α coefficients as a tabulation of ion behavior,

25   independent of mobility device design.

19.   A method as in claim 1 additionally comprising:
                determining alpha parameters for ions mass-identified as
        protonated monomers and proton bound dimmers.

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20.   A method for identifying compounds in a sample comprising:

providing a source of ions representative of the compounds;

causing the ions to be transported through a drift channel, the

5   drift channel having an ion filter associated with it;

applying a high field radio frequency (RF) voltage to the filter,

the high field principally responsible for setting a high electric field

strength within the channel;

applying a compensation voltage to the filter, the compensation

10   voltage principally responsible for selecting ions of a specific mobility

which are allowed to pass through the filter;

a control system for applying the RF voltage and a range

compensation voltages to the filter, and for generating a signature unique

to the compounds according to their high field ion mobility

15   characteristics;

applying at least two different peak RF voltage conditions to the

fitter to observe a response of the sample to at least two different field

conditions; and

identifying the compound as a member of a known species based

20   upon the responses.

21.   A method as in claim 20 wherein the varied RF voltage condition is

frequency.

25   22.   A method as in claim 20 wherein the varied RF voltage condition is its

duty cycle.

23.   A method as in claim 20 wherein the varied RF voltage condition is

pulse amplitude.

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24.   A method as in claim 20 wherein the varied RF voltage condition is
       pulse shape.

5   25.   A method as in claim 21 wherein the change in frequency of the applied
       field is used to selectively filter out a reactant ion peak.

26.   A method as in claim 20 additionally comprising the step of:
           obtaining $\alpha(E)$ from the measurements of compensation voltage
10   versus RF peak voltage.

27.   A method as in claim 20 additionally comprising:
           determining behavior of ketones from hexanone to octanone that
       exhibit plateaus at high fields.

15

28.   A method as in claim 20 wherein the particles are molecules of sulphur
       hexafloride (SF6).

29.   A method as in claim 28 additionally comprising:
20   separately detecting SF6 peaks from reactant ion peaks.

30.   A method for analyzing particles comprising:
           providing a source of particles representative of the compounds;
           passing the particles through a drift channel by applying a high
25   field to separate particles of particular species according to their
       behavior in the drift channel;
           determining a mobility response attribute for at least two
       different high field strengths applied to the drift channel; and

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identifying the particles by comparing the multiple response attributes for the at least two different high field strength conditions.

31.   A method as in claim 30 additionally comprising:
            applying a compensation voltage for selecting particles having a particular attribute to pass completely through the drift channel.

32.   A method as in claim 31 additionally comprising:
            determining an abundance of detected particles across a range of applied fields and compensation voltages to determine an abundance response.

33.   A method as in claim 32 additionally comprising:
            comparing selected peak characteristics in the abundance response for at least two different simultaneously applied field strengths.

34.   A method as in claim 30 additionally comprising:
            determining a mobility dependence upon applied field strength characteristic for various compounds; and
            identifying constituents of a particular sample compound based upon observed mobility behavior in the drift channel.

35.   A method as in claim 34 additionally comprising:
            identifying the sample by comparing a mobility dependence on high field observed curve against the library of such expected curves.

36.   A method as in claim 34 additionally comprising:
            selecting a region of a mobility dependence and determining an attribute of the dependence in that region to identify a sample.

37.   A method as in claim 32 additionally comprising:

    determining a difference in peak position of abundance curves
for two different applied field voltages.

38.   A method as in claim 31 additionally comprising:

    determining a difference in peak height of abundance curves for
two different applied field voltages.

39.   A method as in claim 30 wherein the particles are charged ions and the
high field applied is a high voltage electric field.

40.   A method as in claim 30 wherein the high field applied is a magnetic
field.

41.   A method as in claim 30 additionally comprising:

    identification of compounds is determined via detecting a
dependence of high applied voltage fields and its dependence on ion
mobility.

42.   A method as in claim 30 additionally comprising:

    applying voltages to control mobility behavior through the drift
channel, the voltages applied, including a high field radio frequency
(RF) voltage principally responsible for setting the high electric field
strength within the drift channel, and a compensation voltage principally
responsible for selecting ions of a specific mobility that are allowed to
pass through the drift channel.

43.   A method as in claim 30 additionally comprising:

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determining a mobility characteristic by applying a range of
compensation voltages and peak RF high field voltages to develop a
mobility curve applied RF high field voltage versus peak observed
compensation voltage.

5

44.   A method as in claim 30 wherein the identifying step uses a data
comparison technique selected from the group consisting of table look
up, neural network, and correlation.

10
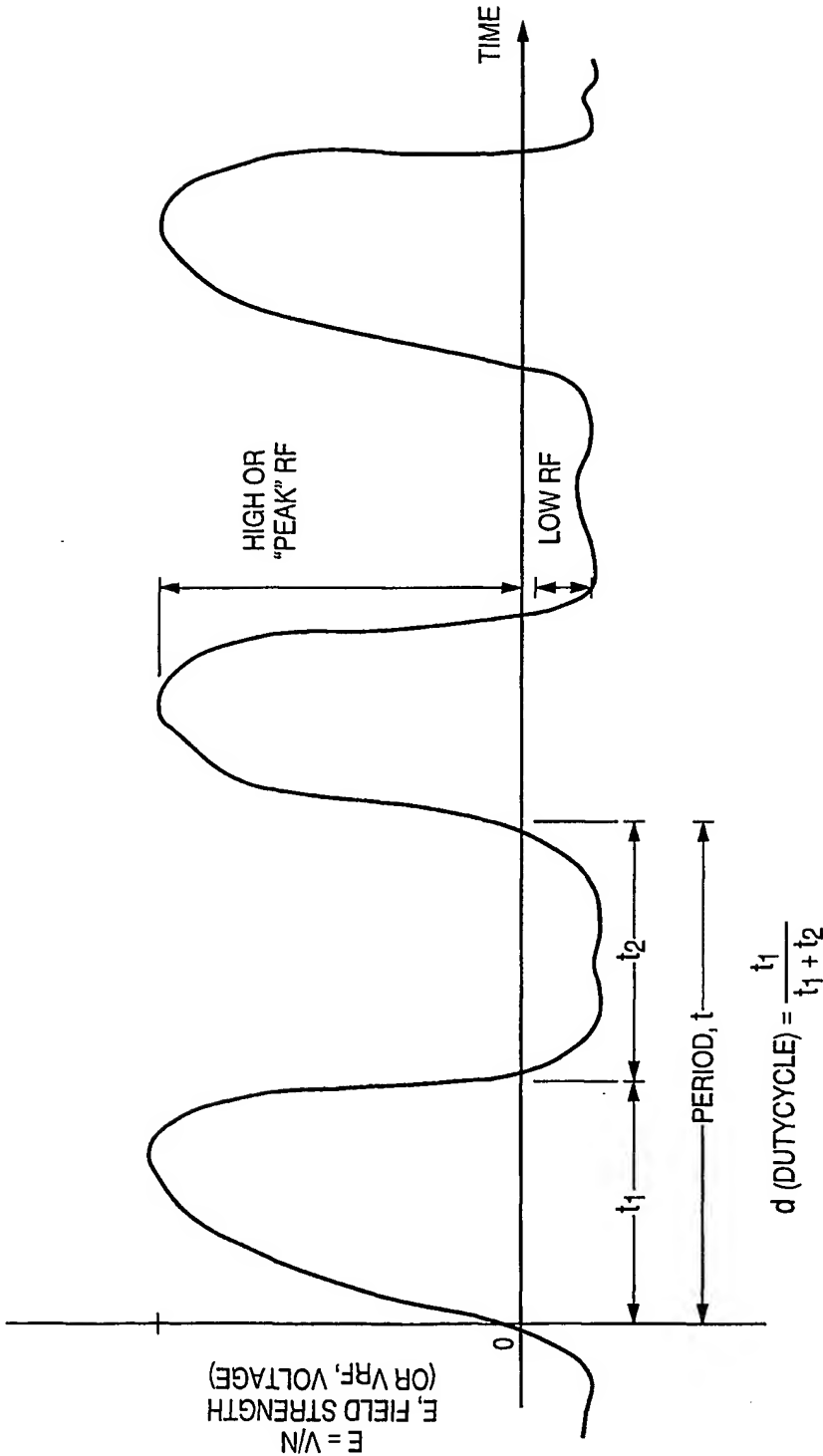
FIG. 1A
(PRIOR ART)
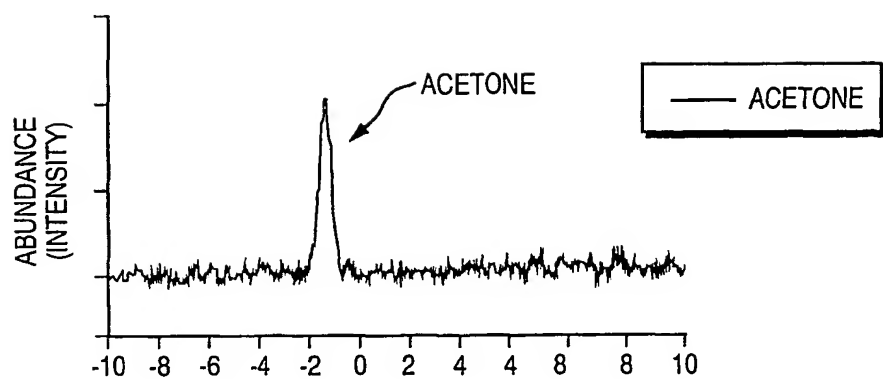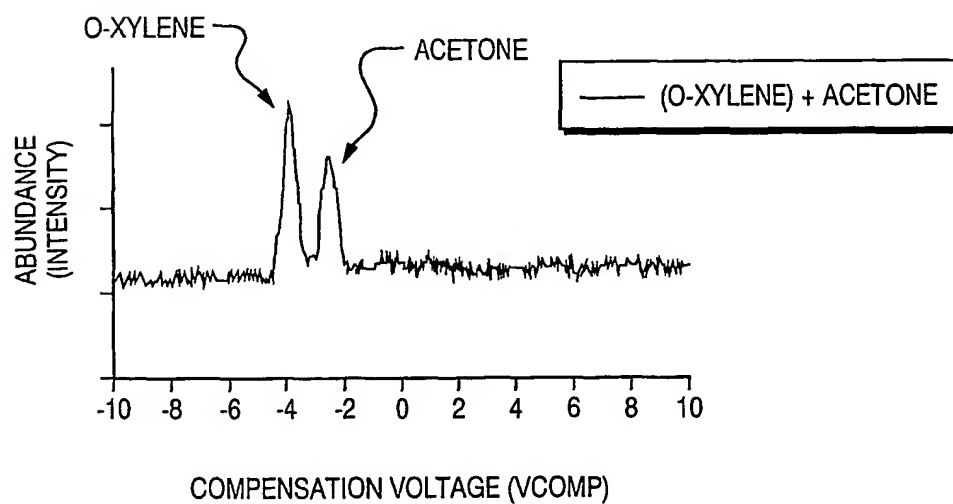
FIG. 1B-1
(PRIOR ART)

FIG. 1B-2
(PRIOR ART)

FIG. 1C
(PRIOR ART)

FIG. 1D
(PRIOR ART)

FIG. 2

6/26

FIG. 3A

1. 33% METHANE, NO SAMPLE
2. 33% METHANE, 6.36E-8 g MERCAPTAN
3. 23% METHANE, 6.36E-8 g MERCAPTAN
4. 15% METHANE, 6.36E-8 g MERCAPTAN
5. 9% METHANE, 6.36E-8 g MERCAPTAN
6. 5% METHANE, 6.36E-8 g MERCAPTAN
7. TRACE METHANE, 6.36E-8 g MERCAPTAN
8. 0% METHANE, 6.36E-8 g MERCAPTAN
9. 0% METHANE, 0 g MERCAPTAN

FIG. 3B

1. 33% METHANE, 0 g MERCAPTAN
2. 33% METHANE, 6.36E-8 g MERCAPTAN
3. 23% METHANE, 6.36E-8 g MERCAPTAN
4. 15% METHANE, 6.36E-8 g MERCAPTAN
5. 9% METHANE, 6.36E-8 g MERCAPTAN
6. 5% METHANE, 6.36E-8 g MERCAPTAN
7. TRACE METHANE, 6.36E-8 g MERCAPTAN
8. 0% METHANE, 6.36E-8 g MERCAPTAN
9. 0% METHANE, 0 g MERCAPTAN

COMPENSATION VOLTAGE (VOLTS)

INTENSITY (ARBITRARY UNITS)

FIG. 3C

COMPENSATION
VOLTAGE

FIG. 3D

Legend:
- - - NO SF6
—— WITH SF6

FIG. 3E

FIG. 3F

COMPENSATION
VOLTAGE

FIG. 3G

FIG. 4

FIG. 5A

FIG. 5B

FIG. 6A

FIG. 6B

FIG. 7

ACETONE

COMPENSATION
V/cm, C

3
4
5
6
7
8
9
10

0   200   400   600   800   1000   1200

DECANONE

S,V
FIELD STRENGTH E/N, td

FIG. 8A

COMPENSATION
V/cm, C

3
4
5
6
7
8
9
10

0   200   400   600   800   1000   1200

S,V
FIELD STRENGTH E/N, td

FIG. 8B

PROTONATED MONOMER

	ACETONE	BUTANONE	PENTANONE	HEXANONE	HEPTANONE	OCTANONE	NONANONE	DECANONE
FORMULA	$C_3H_6OH^+$	$C_4H_8OH^+$	$C_5H_{10}OH^+$	$C_6H_{12}OH^+$	$C_7H_{14}OH^+$	$C_8H_{16}OH^+$	$C_9H_{18}OH^+$	$C_{10}H_{20}OH^+$
m/z(amu)	59	73	87	101	115	129	143	157
α_2[%-Td]	3.14×10^{-3}	2.7×10^{-3}	2.1×10^{-3}	1.7×10^{-3}	1.2×10^{-3}	8.4×10^{-4}	6.5×10^{-4}	4.6×10^{-4}
α_4[%-Td]	-9.54×10^{-8}	-1.4×10^{-7}	-1.2×10^{-7}	-1.1×10^{-7}	-8.8×10^{-8}	-6.9×10^{-8}	-6.6×10^{-8}	-5.2×10^{-8}

PROTON BOUND DIMER

	ACETONE	BUTANONE	PENTANONE	HEXANONE	HEPTANONE	OCTANONE	NONANONE	DECANONE
FORMULA	$(C_3H_6O)_2H^+$	$(C_4H_8O)_2H^+$	$(C_5H_{10}O)_2H^+$	$(C_6H_{12}O)_2H^+$	$(C_7H_{14}O)_2H^+$	$(C_8H_{16}O)_2H^+$	$(C_9H_{18}O)_2H^+$	$(C_{10}H_{20}O)_2H^+$
m/z(amu)	117	145	173	201	229	257	285	303
α_2[%-Td]	1.34×10^{-3}	8.0×10^{-4}	1.9×10^{-4}	1.9×10^{-4}	2.5×10^{-5}	-3.5×10^{-5}	-2.2×10^{-4}	-3.5×10^{-4}
α_4[%-Td]	-1.77×10^{-7}	-1.2×10^{-7}	-6.0×10^{-8}	-8.0×10^{-8}	-6.8×10^{-8}	-6.9×10^{-8}	-4.8×10^{-8}	-3.2×10^{-5}

FIG. 8C

FIG. 9A

FIG. 9B

```
        ┌──────────────┐
        │   KNOWN      │
        │  COMPOUND    │╲ 1000
        └──────────────┘
               ⋮

        ┌──────────────┐
        │ VCOMP, VDISP │╲ 1002
        │ RANGES (b,e,s)│
        └──────────────┘
               │
               ▼
        ┌──────────────┐
        │ VDISP = VDISPb TO │╲ 1004
        │ VDISPe BY VDISPs │◄──────┐
        └──────────────┘          │
               │                  │
               ▼                  │
        ┌──────────────┐          │
        │ VCOMP = VCOMPb TO │╲ 1008│
        │ VCOMPe BY VCOMPs │◄───┐  │
        └──────────────┘      │  │
               │              │  │
               ▼              │  │
        ┌──────────────┐      │  │
        │   STORE      │╲ 1010│  │
        │  RESPONSE (a)│      │  │
        └──────────────┘      │  │
               │              │  │
               ▼   ╱ 1012     │  │
              ╱╲              │  │
             ╱  ╲   NO        │  │
            ╱LAST╲ ───────────┘  │
            ╲ VC ╱              │
             ╲? ╱               │
              ╲╱                │
            YES│                │
               ▼   ╱ 1014       │
              ╱╲                │
             ╱  ╲   NO          │
            ╱LAST╲ ─────────────┘
            ╲ VRF╱
             ╲? ╱
              ╲╱
            YES│
               ▼
        ┌──────────────────────┐
        │  IDENTIFY FEATURES   │╲ 1018
        │ PEAKS (Vc,α)∀ VRF ⇒P │
        └──────────────────────┘
               │
               ○
```

$V_{DISP} = V_{DISPb}$ TO V_{DISPe} BY V_{DISPs} 1004

$V_{COMP} = V_{COMPb}$ TO V_{COMPe} BY V_{COMPs} 1008

STORE RESPONSE (a)   1010

LAST V_C?   1012

LAST V_{RF}?   1014

IDENTIFY FEATURES PEAKS $(V_c, \alpha)^{\forall} V_{RF} \Rightarrow P$ 1018
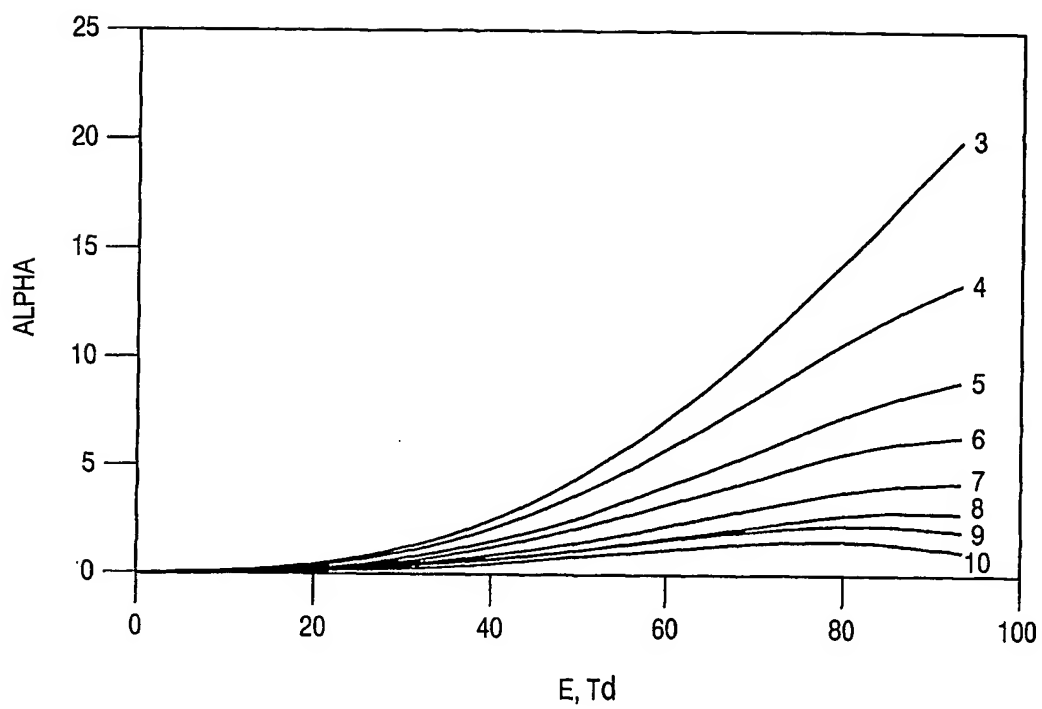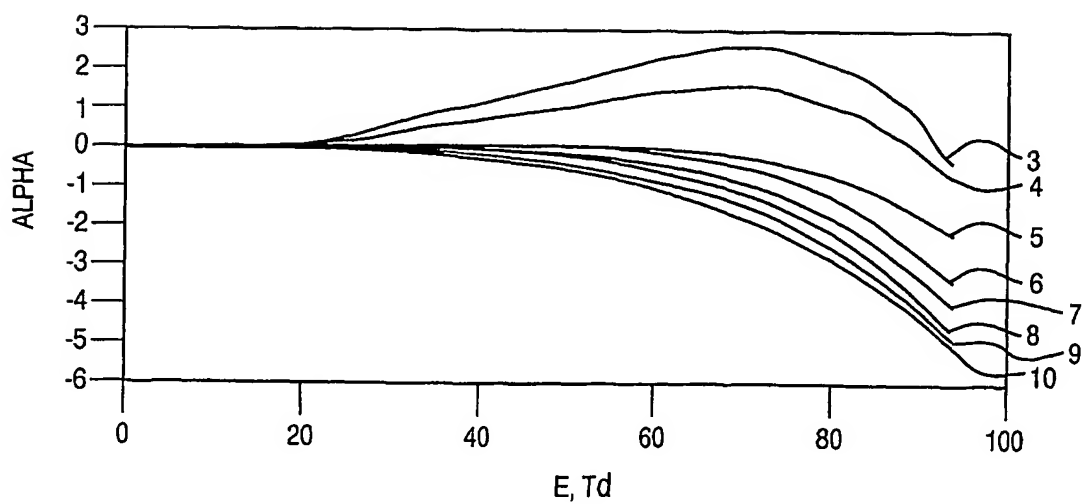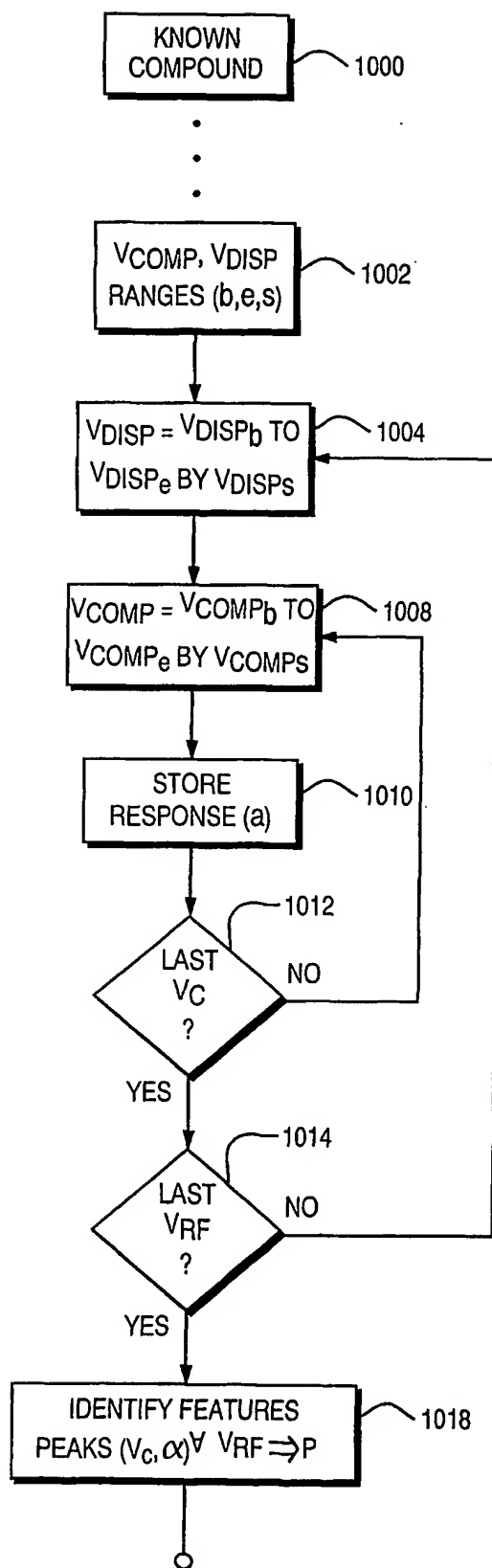
FIG. 10A

COMPOUND ID	
V_{DISP1}	V_{Cl1} a_{ll}
	$\cdots$
	V_{Cln} a_{ln}
$\vdots$	
V_{DISPm}	V_{Cmi} a_{mi}
$V_{DISPm+1}$	V_{Cm-1-1} a_{m-1}
V_{DISPn}	V_{Cm} a_{mn}

P

FIG. 10B

```
        ┌──────────────┐
 1200 ──┤   UNKNOWN    │
        │   COMPOUND   │
        └──────────────┘
              :
              :
        ┌──────────────┐
 1202 ──┤ VDISP, VCOMP │
        │ RANGES (b,e,s)│
        └──────────────┘
        ┌──────────────────┐
 1204 ──┤ VDISP = VDISPb TO │◄──────┐
        │ VDISPe BY VDISPs  │       │
        └──────────────────┘        │
        ┌──────────────────┐        │
 1206 ──┤ VCOMP = VCOMPb TO │◄───┐   │
        │ VCOMPe BY VCOMPs  │    │   │
        └──────────────────┘     │   │
        ┌──────────────┐         │   │
 1210 ──┤    STORE     │         │   │
        │ RESPONSES a  │         │   │
        └──────────────┘         │   │
            ◇ LAST              │   │
 1212 ──    ◇  Vc  ◇────────────┘   │
            ◇  ?  ◇                 │
            ◇ LAST              │
 1214 ──    ◇  VRF ◇────────────────┘
            ◇  ?  ◇
        ┌──────────────────────┐
 1220 ──┤ IDENTIFY FEATURES     │
        │ (PEAKS Vc,a) ∀ VDISP⇒P'│
        └──────────────────────┘
        ┌──────────────┐
 1230 ──┤   ∀     P'   │◄──────┐
        └──────────────┘        │
        ┌──────────────┐        │
 1240 ──┤  COMPARE P   │────────┘
        │ VS. P' SCORE │
        └──────────────┘
        ┌──────────────┐     ┌──────────────┐
 1250 ──┤  PICK BEST   │────►│   LOOKUP     │── 1260
        │    MATCH     │     │  COMPOUND    │──○
        └──────────────┘     │    FIELD     │
                             └──────────────┘
```

FIG. 10C

SUBSTITUTE SHEET (RULE 26)

$\cdot$
$\cdot$
$\cdot$

○

| FOR $\forall \in P$ | — 1020 |

| $Z = \{V_{C11}, a_{11},\} \{V_{c12}, a_{12}\} \cdots \{V_{C1m}, a_{1m}\}$ | — 1022 |

| CURVE FIT
$Z \Rightarrow y^2 = \beta x^2 + \gamma, (\beta, \gamma)$ | — 1024 |

| STORE
β, γ | — 1026 |

$\cdot$
$\cdot$
$\cdot$

| FOR $\forall \in P'$ | — 1270 |

| CURVE FIT
$Z' = \beta' + \gamma'$ | — 1272 |

| MATCH β', γ'
TO BEST β, γ | — 1274 |

$\cdot$
$\cdot$
$\cdot$

FIG. 10D

COMPOUND ID				
V_{RF1}	$V_{C11}, a_{11}, \ell_{11}$	$V_{C12}, a_{12}, \ell_{12}$	$\cdots$	$V_{C1n}, a_{1n}, \ell_{1n}$
V_{RF2}	$V_{C21}, a_{21}, \ell_{21}$	$V_{C22}, a_{22}, \ell_{22}$		$V_{C2n}, a_{2n}, \ell_{2n}$
V_{RFm}	$V_{Cm1}, a_{m1}, \ell_{m1}$	$V_{Cm2}, a_{m2}, \ell_{m2}$	$\cdots$	$V_{Cmn}, a_{mn}, \ell_{mn}$
V_{FRAG}				

$\ell = \{MONOMER, CLUSTER, RIP\}$

FIG. 10E

P

・
・
・

┌── 1320

PEAK
DETECT
WITH NO   YES ℓ = RIP
COMPOUND   ──────▶
APPLIED
?

・
・
・

┌── 1310

┌── 1311

PEAK
SHIFT RIGHT   YES ℓ = CLUSTER
AS V$_{RF}$ ──────▶
?

│
│ NO
│   ┌── 1312
▼

ℓ = MONOMER

FIG. 10F

$\forall \in P'$ — 1280

COMPARE MONOMER (P,P') — 1282

SCORE S_m — 1284

COMPARE CLUSTER (P,P') — 1286

SCORE S_c — 1288

(f) $S_f = W_m S_m + W_c S_c$ — 1290
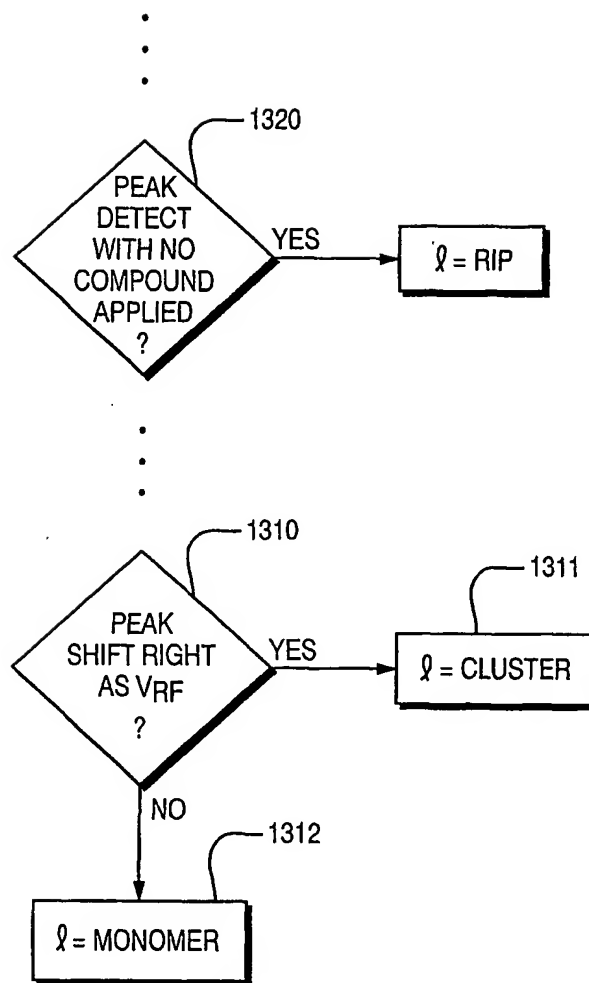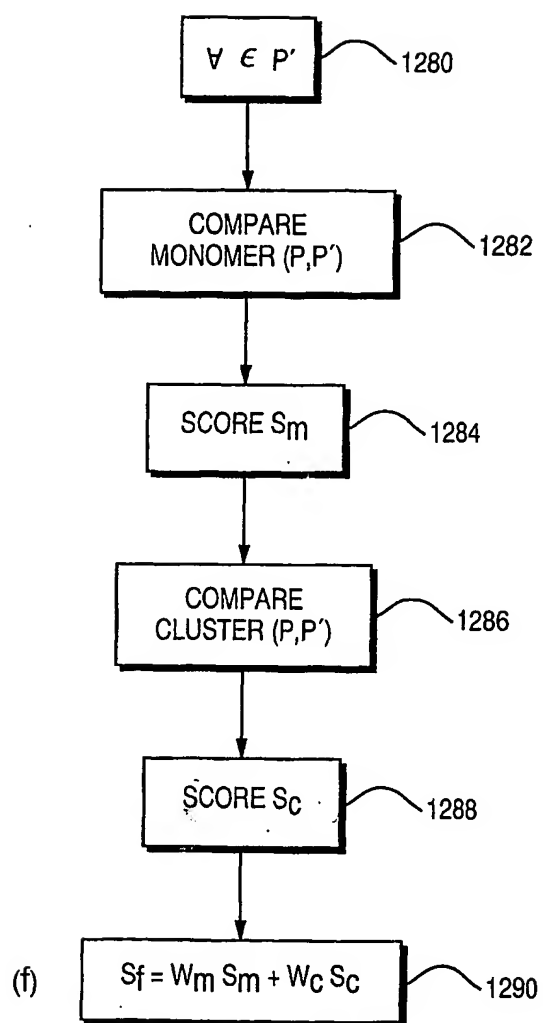
FIG. 10G

INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7   G01N27/64

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7   G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	the whole document	28,29
X	WO 01 35441 A (DRAPER LAB CHARLES S) 17 May 2001 (2001-05-17)	1-4,8,9, 20,22, 27, 30-36, 39,42
	page 15, paragraph 1; figures 10,11 page 10, paragraph 2 page 17, line 5 - line 8	

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| [X] | Further documents are listed in the continuation of box C. | [X] | Patent family members are listed in annex. |

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 October 2002	06/11/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Strohmayer, B

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
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